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| | | <u> </u> |
| (54) Title: HUMAN PROTEINS HAVING TRANSMEM | BRAN | E DOMAINS AND DNAS ENCODING THESE PROTEINS |
| (57) Abstract | | |
| Proteins comprising any of the amino acid sequences of the nucelotide sequences of SEQ ID NOS: 19 to 36 are | | 2 ID NOS: 1 to 18 and DNAs encoding said proteins and comprising any ed. |
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DESCRIPTION

Human Proteins Having Transmembrane Domains and DNAs Encoding These Proteins

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FIELD OF THE INVENTION

The present invention relates to human proteins having transmembrane domains and cDNAs encoding these proteins. The membrane proteins of this invention can be used as pharmaceuticals or as antigens for preparing antibodies against said proteins. The cDNAs of the invention can be used as probes for the gene diagnosis and gene sources for the gene therapy. The cDNAs can also be used as gene sources for large-scale production of the membrane proteins encoded by the same. The cells into which the genes encoding the membrane proteins are introduced for expression of such membrane proteins in large amounts can be used for detection of the corresponding ligands, screening of low molecular weight medicines, etc.

20 BACKGROUND OF THE INVENTION

Membrane proteins play important roles as signal receptors, ion channels, transporters, etc. for the material transportation or information transmission mediated by the cell membrane. For instance, they are known to serve as receptors for various cytokines, ion channels for sodium ion, potassium ion, chloride ion, etc., transporters for saccharides and amino acids, and so on. The genes for many of them have been cloned already.

In recent years, it was clarified that the abnormalities

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of these membrane proteins are related to a number of hitherto cryptogenic diseases. For example, a gene for a membrane protein having 12 transmembrane domains was identified as the gene responsible for cystic fibrosis [Rommens, J. M. et al., 5 Science 245: 1059-1065 (1989)]. It was also clarified that several membrane proteins act as the receptors when a virus infects the cells. For example, HIV-1 was revealed to infect into the cells through the mediation of a membrane protein fusin, a membrane protein on the T-cell membrane, having a CD-4 antigen and 7 transmembrane domains [Feng, Y. et al., Science 272: 872-877 (1996)]. Therefore, the discovery of new membrane proteins is anticipated to lead to the elucidation of the causes of many diseases, and the isolation of new genes coding for the membrane proteins is desired.

Heretofore, owing to the difficulty in their purification, many of membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises transfection of a cDNA library in the animal cells to express the cDNA and detection of the cells expressing the target membrane protein on the membrane by an immunological technique using an antibody or a physiological technique for the change in the membrane permeability. However, this method is applicable only to cloning of a gene for a membrane protein with a known function.

In general, membrane proteins possess hydrophobic transmembrane domains inside the proteins which are synthesized in
the ribosome. Said domains remain in the phospholipid to be
trapped in the membrane. Accordingly, the evidence of the cDNA
for encoding the membrane protein is provided by determination

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of the whole base sequence of a full-length cDNA and detection of highly hydrophobic transmembrane domains in the amino acid sequence of the protein encoded by said cDNA.

As a result of the extensive study, there have successful
ly been obtained human proteins having transmembrane domains,
particularly comprising any of the amino acid sequences of SEQ

ID NOS: 1 to 18, by cloning cDNAs coding for proteins having
transmembrane domains, particularly comprising any of the
nucleotide sequences of SEQ ID NOS: 19 to 36, from a human

full-length cDNA bank. The present invention is based on the
above success.

SUMMARY OF THE INVENTION

A main object of the present invention is to provide novel
human proteins having transmembrane domains, particularly
comprising any of the amino acid sequences of SEQ ID NOS: 1 to
18. Another object of this invention is to provide DNAs coding
for said novel proteins, particularly comprising any of the
nucleotide sequences of SEQ ID NOS: 19 to 36. A further object
of the invention is to provide expression vectors capable of in
vitro translating said DNAs or expressing said DNAs in
eukaryotic cells. A still further object of the invention is
to provide transformed eukaryotic cells capable of expressing
said DNAs to produce said proteins.

In one embodiment, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ ID NOS: 1 to 18 and their fragments.

In another embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.

In a further embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.

10 BRIEF DESCRIPTION OF DRAWINGS

- Figure 1: A figure depicting the structure of the secretory signal sequence detection vector pSSD3.
- Figure 2: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01263.
- 15 Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01299.
 - Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01347.
- Figure 5: A figure depicting the hydrophobicity/hydrophi-20 licity profile of the protein encoded by clone HP01440.
 - Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01526.
 - Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10230.
- 25 Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10389.
 - Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10408.
 - Figure 10: A figure depicting the hydrophobicity/hydro-

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philicity profile of the protein encoded by clone HP10412.

Figure 11: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10413.

Figure 12: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10415.

Figure 13: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10419.

Figure 14: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10424.

10 Figure 15: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10428.

Figure 16: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10429.

Figure 17: A figure depicting the hydrophobicity/hydro15 philicity profile of the protein encoded by clone HP10432.

Figure 18: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10433.

Figure 19: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10480.

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BEST MODE FOR CARRING OUT INVENTION

The proteins of the present invention can be obtained, for example, by isolation from human organs, cell lines, etc., by chemical synthesis on the basis of the amino acid sequences as herein disclosed, or by recombinant DNA technology using the DNA encoding the transmembrane domains of the invention. Among them, adoption of the recombinant DNA technology is preferred. Specifically, each of the proteins may be prepared by in vitro transcription of a vector comprising the cDNA of the invention

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to make RNA and in vitro translation using this RNA as a template to accomplish in vitro expression. Also, each of the proteins may be prepared in a large amount by the use of Escherichia coli, Bacillus subtilis, yeasts, animal cells, etc. 5 comprising a suitable expression vector having the DNA encoding such protein.

In the case of producing the protein of the invention by the use of a microorganism such as Escherichia coli, the translation region of the cDNA of the invention is constructed in an expression vector having an origin, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator, etc. that can be replicated in the microorganism and, after transformation of the host cells with said expression vector, the resultant transformant is incubated, whereby the protein 15 encoded by said cDNA can be produced in a large amount in the microorganism. In that case, a protein fragment containing an optional region can be obtained by performing the expression with inserting an initiation codon and a termination codon before and after the optional translation region. Alternative-20 ly, a fusion protein with another protein can be expressed. Only a protein portion encoding said cDNA can be obtained by cleavage of said fusion protein with an appropriate protease.

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For production of the protein of the invention by expression of DNA coding for such protein in eukaryotic cells, 25 the translation region of said cDNA may be recombined into an expression vector for eukaryotic cells having a promoter, a splicing domain, a poly(A) addition site, etc., followed by introduction into eukaryotic cells so that the protein of the invention is produced as a membrane protein on the cell

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membrane surface. Examples of the expression vector are pKA1, pED6_dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, etc. As the eukaryotic cells, there are exemplified mammalian animal culture cells (e.g. simian kidney cells COS7, chinese hamster ovary cells CHO), budding yeasts, Schizosaccharomyces pombe, silkworm cells, Xenopus laevis egg cells, etc., but any other eukaryotic cells may also be used insofar as the protein of the invention can be expressed on the membrane surface. In order to introduce the expression vector into eukaryotic cells, there may be adopted any conventional procedure such as electroporation, calcium phosphate method, liposome method or DEAE dextran method.

The proteins of the present invention include peptide fragments (5 or more amino acid residues) containing any 15 partial amino acid sequence of the amino acid sequences of SEQ ID NOS: 1 to 18. These fragments can be used as antigens for preparation of the antibodies. Also, the proteins of the invention that have signal sequences appear in the form of maturation proteins on the cell surface, after the signal 20 sequences are removed. Therefore, these maturation proteins shall come within the scope of the present invention. The Nterminal amino acid sequences of the maturation proteins can be easily identified by using the method for the cleavage-site determination in a signal sequence [Japan Patent Kokai No. 25 187100/96]. Further, many membrane proteins are subjected to the processing on the cell surface to be converted to the secretor forms. These secretor proteins or peptides shall come within the scope of the present invention. When glycosylation sites are present in the amino acid sequences, expression in

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appropriate animal cells affords glycosylated proteins. Therefore, these glycosylated proteins or peptides also shall come within the scope of the invention.

The DNAs of the invention include all DNAs encoding the 5 above-mentioned proteins. Said DNAs can be obtained using the method by chemical synthesis, the method by cDNA cloning, and so on.

Each of the cDNAs of the invention can be cloned from, for example, the cDNA libraries of the human cell origin. The cDNA 10 is synthesized using as a template a poly(A) + RNA extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the culture cells. The cDNA can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, 15 P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)] as illustrated in Examples in order to obtain a full-length clone in an effective manner.

The primary selection of a cDNA encoding a human protein having transmembrane domains is performed by the sequencing of a partial base sequence of the cDNA clone selected at random from the cDNA libraries, sequencing of the amino acid sequence encoded by the base sequence, and recognition of the presence 25 or absence of hydrophobic site(s) in the resulting N-terminal amino acid sequence region. Next, the secondary selection is carried out by determination of the whole base sequence by the sequencing and the protein expression by the in vitro translation. The ascertainment of the cDNA of the present

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invention for encoding the protein having the secretory signal sequence is performed by using the signal sequence detection method [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. In other words, the ascertainment for the coding portion of the inserted cDNA fragment to function as a signal sequence is provided by fusing a cDNA fragment encoding the N-terminus of the target protein with a cDNA encoding the protease domain of urokinase and then expressing the resulting cDNA in COS7 cells to detect the urokinase activity in the cell culture medium. On the other hand, the N-terminal region is judged to remain in the membrane in the case where the urokinase activity is not detected in the cell culture medium.

The cDNAs of the invention are characterized by containing any of the nucleotide sequences of SEQ ID NOS: 19 to 36 or any of the nucleotide sequences of SEQ ID NOS: 37 to 54. Table 1 summarizes the clone number (HP number), the cells affording the cDNA, the total nucleotide number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

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Table 1

| 5 | Sequence Number | HP Number | Cells | Number of Nucleotides | Number of Amino Acid Residues |
|----|--------------------|--------------|----------------|--------------------------|-------------------------------------|
| 10 | 1, 19, 37 | HP01263 | Liver | 1502 | 382 |
| 10 | 2, 20, 38 | HP01299 | Liver | 1349 | 317 |
| | 3, 21, 39 | HP01347 | Liver | 1643 | 296 |
| 15 | 4, 22, 40 | HP01440 | Stomach cancer | 729 | 197 |
| | 5, 23, 41 | HP01526 | Stomach cancer | 1322 | 221 |
| 20 | 6, 24, 42 | HP10230 | Stomach cancer | 3045 | 251 |
| 20 | 7, 25, 43 | HP10389 | КВ | 653 | 106 |
| | 8, 26, 44 | HP10408 | Stomach cancer | 439 | 78 |
| 25 | 9, 27, 45 | HP10412 | Stomach cancer | 1131 | 314 |
| | 10, 28, 46 | HP10413 | Stomach cancer | 1875 | 195 |
| 30 | 11, 29, 47 | HP10415 | Stomach cancer | 1563 | 462 |
| | 12, 30, 48 | HP10419 | Stomach cancer | 2030 | 247 |
| | 13, 31, 49 | HP10424 | Stomach cancer | 493 | 113 |
| 35 | 14, 32, 50 | HP10428 | КВ | 2044 | 365 |
| | 15, 33, 51 | HP10429 · | Stomach cancer | 1043 | 226 |
| 40 | 16, 34, 52 | HP10432 | Liver | 972 | 129 |
| 70 | 17, 35, 53 | HP10433 | Liver | 695 | 163 |
| | 18, 36, 54 | HP10480 | Stomach cancer | 1914 | 193 |

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Hereupon, the same clone as any of the cDNAs of the invention can be easily obtained by screening of the cDNA libraries constructed from the cell line or the human tissues employed in the invention, by the use of an oligonucleotide probe synthesized on the basis of the corresponding cDNA nucleotide sequence of SEQ ID NOS: 37 to 54.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Therefore, any cDNA that is subjected to insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides

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in SEQ ID NOS: 37 to 54 shall come within the scope of the invention.

In a similar manner, any protein that is produced by these modifications comprising insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides shall come within the scope of the present invention, as far as said protein possesses the activity of the corresponding protein having the amino acid sequence of SEQ ID NOS: 1 to 18.

The cDNAs of the invention include cDNA fragments (more than 10 bp) containing any partial nucleotide sequence of the nucleotide sequence of SEQ ID NOS: 19 to 36 or of the nucleotide sequence of SEQ ID NOS: 37 to 54. Also, DNA fragments consisting of a sense chain and an anti-sense chain shall come within this scope. These DNA fragments can be used as the probes for the gene diagnosis.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate

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genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

5 Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave 10 the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that 15 have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified 20 genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 Bl, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to 25 the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through

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insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 5 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are Such organisms are useful for the development of mammals. non-human models for the study of disorders involving the 15 corresponding gene(s), and for the development of assay systems for the identi fication of molecules that interact with the protein product(s) of the corresponding gene(s).

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Where the protein of the present invention membrane-bound (e.g., is a receptor), the present invention 20 also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be 25 identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at

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least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences

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complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably being the stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example,

Table 2

| Stringency | Polynucleotide | Hybrid | Hybridization Temperature | Wash |
|------------|----------------|-------------------|---------------------------|-------------------------|
| Condition | Hybrid | Length | and Buffer [†] | Temperature |
| | | (bp) [‡] | | and Buffer† |
| A | DNA : DNA | ≥50 | 65°C; 1×SSC -or- | 65℃; 0.3×SSC |
| | | | 42℃; 1×SSC,50% formamide | |
| В | DNA : DNA | <50 | T _B *; 1×SSC | T_{B} *; 1×SSC |
| C | DNA: RNA | ≥50 | 67℃; 1×SSC -or- | 67°C; 0.3×SSC |
| | | | 45°C; 1×SSC,50% formamide | |
| D | DNA: RNA | <50 | T _D *; 1×SSC | T _D *; 1×SSC |
| E | RNA: RNA | ≥50 | 70℃; 1×SSC -or- | 70°C; 0.3×SSC |
| | • | | 50℃; 1×SSC,50% formamide | |
| F | RNA: RNA | <50 | T _F *; 1×SSC | T _F *; 1×SSC |
| G | DNA : DNA | ≥50 | 65°C; 4×SSC -or- | 65℃; 1×SSC |
| | | | 42°C; 4×SSC,50% formamide | |
| H | DNA : DNA | <50 | T _H *; 4×SSC | T _H *; 4×SSC |
| I | DNA : RNA | ≥50 | 67°C; 4×SSC -or- | 67℃; 1×SSC |
| | | | 45℃; 4×SSC,50% formamide | · |
| J | DNA: RNA | <50 | T _J *; 4×SSC | T _J *; 4×SSC |
| K | RNA : RNA | ≥50 | 70°C; 4×SSC -or- | 67°C; 1×SSC |
| | | V / | 50°C; 4×SSC,50% formamide | |
| L | RNA: RNA | <50 | T _L *; 2×SSC | T _L *; 2×SSC |
| M | DNA : DNA | ≥50 | 50℃; 4×SSC -or- | 50°C; 2×SSC |
| | | | 40℃; 6×SSC,50% formamide | , |
| N | DNA : DNA | <50 | T _N *; 6×SSC | T _N *; 6×SSC |
| 0 | DNA : RNA | ≥50 | 55°C; 4×SSC -or- | 55°C; 2×SSC |
| | | | 42℃; 6×SSC,50% formamide | |
| P | DNA : RNA | <50 | T _P *; 6×SSC | T _P *; 6×SSC |
| Q | RNA: RNA | ≥50 | 60°C; 4×SSC -or- | 60°C; 2×SSC |
| , | | | 45°C; 6×SSC,50% formamide | , |
| R | RNA: RNA | <50 | T _R *; 4×SSC | T _R *; 4×SSC |

- ‡: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.
- †: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH₂PO₄, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.
- * T_B T_R : The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m (°C)=2(#of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m (°C)=81.5 + 16.6(log₁₀[Na⁺]) + 0.41 (%G+C) (600/N), where N is the number of bases in the hybrid, and [Na⁺] is the concentration of sodium ions in the hybridization buffer ([Na⁺] for 1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are

provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory

5 Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and

Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc.,

sections 2.10 and 6.3-6.4, incorporated herein by reference.

10 Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more

preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of

the present invention to which it hybridizes, and has at least

15 60% sequence identity (more

preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the

polynucleotide of the present invention to which it hybridizes, where sequence identity is

20 determined by comparing the sequences of the hybridizing polynucleotides when aligned so as

to maximize overlap and identity while minimizing sequence gaps.

25 EXAMPLE

The present invention is embodied in more detail by the following examples, but this embodiment is not intended to restrict the present invention. The basic operations and the enzyme reactions with regard to the DNA recombination are

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Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo Co., Ltd. The manufacturer's instructions were used for the buffer compositions as well as for the reaction conditions, in each of the enzyme reactions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

10 (1) Preparation of Poly(A) + RNA

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The epidermoid carcinoma cell line KB (ATCC CRL 17), tissues of stomach cancer delivered by the operation, and liver were used for human cells to extract mRNAs. The cell line was cultured by a conventional procedure.

15 After about 1 g of human tissues was homogenized in 20 ml of a 5.5 M guanidinium thiocyanate solution, total mRNAs were prepared in accordance with the literature [Okayama, H. et al., "Methods in Enzymology" Vol. 164, Academic Press, 1987]. These mRNAs were subjected to chromatography using an oligo(dT)-20 cellulose column washed with 20 mM Tris-hydrochloric acid buffer solution (pH 7.6), 0.5 M NaCl, and 1 mM EDTA to obtain a poly(A)⁺ RNA in accordance with the above-mentioned literature.

(2) Construction of cDNA Library

To a solution of 10 μg of the above-mentioned poly(A)⁺ RNA in 100 mM Tris-hydrochloric acid buffer solution (pH 8) was added one unit of an RNase-free, bacterium-origin alkaline phosphatase and the resulting solution was allowed to react at 37°C for one hour. After the reaction solution underwent the

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phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 50 mM sodium acetate (pH 6), 1 mM EDTA, 0.1% 2-mercaptoethanol, and 0.01% Triton X-100. Thereto was added one unit of a tobacco-origin pyrophosphatase (Epicenter Technologies) and the resulting solution at a total volume of 100 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a decapped poly(A)[†] RNA solution.

To a solution of the decapped poly(A)⁺ RNA and 3 nmol of a DNA-RNA chimeric oligonucleotide (5'-dG-dG-dG-dG-dA-dA-dT-dT-dC-dG-dA-G-G-A-3') in a mixed aqueous solution of 50 mM Trishydrochloric acid buffer solution (pH 7.5), 0.5 mM ATP, 5 mM MgCl₂, 10 mM 2-mercaptoethanol, and 25% polyethylene glycol were added 50 units of T4 RNA ligase and the resulting solution at a total volume of 30 µl was allowed to react at 20°C for 12 hours. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thusobtained pellets were dissolved in water to obtain a chimeric oligo-capped poly(A)⁺ RNA.

After the vector pKAl developed by the present inventors (Japanese Patent Kokai Publication No. 1992-117292) was digested with KpnI, an about 60-dT tail was inserted by a terminal transferase. This product was digested with EcoRV to remove the dT tail at one side and the resulting molecule was used as a vectorial primer.

After 6 μg of the previously-prepared chimeric oligocapped poly(A)⁺ RNA was annealed with 1.2 μg of the vectorial

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primer, the product was dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 8.3), 75 mM KCl, 3 mM $MgCl_2$, 10 mM dithiothreitol, and 1.25 mM dNTP (dATP + dCTP + dGTP + dTTP), mixed with 200 units of a reverse transferase (GIBCO-BRL), and the resulting solution at a total volume of 20 µl was allowed to react at 42°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in a mixed solution of 50 mM Tris-hydrochloric acid 10 buffer solution (pH 7.5), 100 mM NaCl, 10 mM MgCl2, and 1 mM dithiothreitol. Thereto were added 100 units of EcoRI and the resulting solution at a total volume of 20 μ l was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol 15 precipitation, the obtained pellets were dissolved in a mixed solution of 20 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM KCl, 4 mM MgCl₂, 10 mM (NH₄)₂SO₄, and 50 μ g/ml bovine serum albumin. Thereto were added 60 units of Escherichia coli DNA ligase and the resulting solution was 20 allowed to react at 16°C for 16 hours. To the reaction solution were added 2 µl of 2 mM dNTP, 4 units of Escherichia coli DNA polymerase I, and 0.1 unit of Escherichia coli DNase H and the resulting solution was allowed to react at 12°C for one hour and then at 22°C for one hour.

Next, the cDNA-synthesis reaction solution was used to transform *Escherichia coli* DH12S (GIBCO-BRL). The transformation was carried out by the electroporation method. A portion of the transformant was inoculated on a 2xYT agar culture medium containing 100 µg/ml ampicillin, which was

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incubated at 37°C overnight. A colony grown on the culture medium was randomly picked up and inoculated on 2 ml of the 2xYT culture medium containing 100 $\mu g/ml$ ampicillin, which was incubated at 37°C overnight. The culture medium was centrifuged 5 to separate the cells, from which a plasmid DNA was prepared by the alkaline lysis method. After the plasmid DNA was doubledigested with EcoRI and NotI, the product was subjected to 0.8% agarose gel electrophoresis to determine the size of the cDNA insert. In addition, by the use of the obtained plasmid as a 10 template, the sequence reaction using M13 universal primer labeled with a fluorescent dye and Taq polymerase (a kit of Applied Biosystems Inc.) was carried out and the product was analyzed by a fluorescent DNA-sequencer (Applied Biosystems Inc.) to determine the base sequence of the cDNA 5'-terminal of 15 about 400 bp. The sequence data were filed as a homo-protein cDNA bank data base.

(3) Selection of cDNAs Encoding Proteins Having
Transmembrane Domains

The base sequence registered in the homo-protein cDNA bank

20 data base was converted to three frames of amino acid sequences
and the presence or absence of an open reading frame (ORF)
beginning from the initiation codon. Then, the selection was
made for the presence of a signal sequence that is
characteristic to a secretory protein at the N-terminal of the

25 portion encoded by ORF. These clones were sequenced from the
both 5' and 3' directions by using the deletion method to
determine the sequence of the whole base sequence. The
hydrophobicity/hydrophilicity profiles were obtained for
proteins encoded by ORF by the Kyte-Doolittle method [Kyte, J.

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& Doolittle, R. F., J. Mol. Bio. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. In the case in which there is a hydrophobic region of putative transmembrane domain(s) in the amino acid sequence of an encoded protein, this protein was considered as a membrane protein.

(4) Construction of Secretory Signal Detection Vector pSSD3

One microgram of pSSD1 carrying the SV40 promoter and a 10 cDNA encoding the protease domain of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)] was digested with 5 units of Bg1II and 5 units of EcoRV. Then, after dephosphorylation at the 5' terminal by the CIP treatment, a DNA fragment of about 4.2 kbp was purified by cutting off from the gel of agarose gel electrophoresis.

Two oligo DNA linkers, L1 (5'-GATCCCGGGTCACGTGGGAT-3') and L2 (5'-ATCCCACGTGACCCGG-3'), were synthesized phosphorylated by T4 polynucleotide kinase. After annealing of the both linkers, followed by ligation with the previously-20 prepared pSSD1 fragment by T4 DNA ligase, Escherichia coli JM109 was transformed. A plasmid pSSD3 was prepared from the transformant and the objective recombinant was confirmed by the determination of the base sequence of the linker-inserted fragment. Figure 1 illustrates the structure of the thus-25 obtained plasmid. The present plasmid vector carries three types of blunt-end formation restriction enzyme sites, SmaI, PmaCI, and EcoRV. Since these cleavage sites are positioned in succession at an interval of 7 bp, selection of an appropriate site in combination of three types of frames for the inserting

cDNA allows to construct a vector expressing a fusion protein.

(5) Functional Verification of Secretory Signal Sequence Whether the N-terminal hydrophobic region in the secretory protein clone candidate obtained in the above-mentioned steps functions as the secretory signal sequence was verified by the method described in the literature [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. First, the plasmid containing the target cDNA was cleaved at an appropriate restriction enzyme site that existed at the downstream of the portion 10 expected for encoding the secretory signal sequence. In the case in which this restriction enzyme site was a protruding terminus, the site was blunt-ended by the Klenow treatment or treatment with the mung-bean nuclease. Digestion with HindIII was further carried out and a DNA fragment containing the SV40 15 promoter and a cDNA encoding the secretory sequence at the downstream of the promoter was separated by agarose gel electrophoresis. This fragment was inserted between the pSSD3 HindIII site and a restriction enzyme site selected so as to match with the urokinase-coding frame, thereby constructing a 20 vector expressing a fusion protein of the secretory signal portion of the target cDNA and the urokinase protease domain.

After Escherichia coli (host: JM109) bearing the fusionprotein expression vector was incubated at 37°C for 2 hours in
2 ml of the 2xYT culture medium containing 100 μg/ml
25 ampicillin, the helper phage M13KO7 (50 μl) was added and the
incubation was continued at 37°C overnight. A supernatant
separated by centrifugation underwent precipitation with
polyethylene glycol to obtain single-stranded phage particles.
These particles were suspended in 100 μl of 1 mM Tris-0.1 mM

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EDTA, pH 8 (TE). Also, there was used as a control a suspension of single-stranded particles prepared in the same manner from the vector pLA1-UPA containing pSSD3 and a full-length cDNA of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)].

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simian-kidney-origin culture cells, The COS7, were incubated at 37°C in the presence of 5% CO2 in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% bovine fetus albumin. Into a 6-well plate (Nunc Inc., 3 cm in the well 10 diameter) were inoculated 1×10^5 COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO2. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the cells were added 1 µl of the single-stranded 15 phage suspension, 0.6 ml of the DMEM culture medium, and 3 µl of TRANSFECTAMTM (IBF Inc.) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO2. After the sample solution was removed, the cell surface was washed 20 with TDMEM, 2 ml per well of DMEM containing 10% bovine fetus albumin was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO₂.

To 10 ml of 50 mM phosphate buffer solution (pH 7.4) containing 2% bovine fibrinogen (Miles Inc.), 0.5% agarose, and 1 mM potassium chloride were added 10 units of human thrombin (Mochida Pharmaceutical Co., Ltd.) and the resulting mixture was solidified in a plate of 9 cm in diameter to prepare a fibrin plate. Ten microliters of the culture supernatant of the

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transfected COS7 cells were spotted on the fibrin plate, which was incubated at 37°C for 15 hours. The diameter of the thusobtained clear circle was taken as an index for the urokinase activity. In the case in which a cDNA fragment codes for the
amino acid sequence that functions as a secretory signal sequence, a fusion protein is secreted to form a clear circle
by its urokinase activity. Therefore, in the case in which a
clear circle is not formed, the fusion protein remains as
trapped in the membrane and the cDNA fragment is considered to
code for a transmembrane domain.

(6) Protein Synthesis by In Vitro Translation

The plasmid vector carrying the cDNA of the present invention was utilized for the transcription/translation by the T_NT rabbit reticulocyte lysate kit (Promega Biotec). In this 15 case, [35]methionine was added and the expression product was labeled with the radioisotope. All reactions were carried out by following the protocols attached to the kit. Two micrograms of the plasmid was allowed to react at 30°C for 90 minutes in total 25 ml of a reaction solution containing 12.5 µl of the 20 T_NT rabbit reticulocyte lysate, 0.5 μ l of the buffer solution (attached to the kit), 2 µl of an amino acid mixture (methionine-free), 2 μ l (0.37 MBq/ μ l) of [35 S]methionine (Amersham Corporation), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. To 3 μl of the reaction solution was added 2 μl of an SDS sampling buffer (125 mM Tris-hydrochloric acid suffer solution, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting solution was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of

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the translation product was determined by carrying out the autoradiography.

(7) Expression in COS7

Escherichia coli bearing a vector expressing the protein

of the invention was infected with helper phage M13KO7, and single-stranded phage particles were obtained according to the method as stated above. Using the thus obtained phages, each expression vecotr was introduced into simian-kidney-origin culture cells COS7 in the manner as stated above. After incubation at 37 °C for 2 days in the presence of 5 % CO₂, further incubation was carried out in a medium containing [35S]cysteine or [35S]methionine for 1 hour. The cells were collected, dissolved and then subjected to SDS-PAGE whereby a band corresponding to the expression product of each protein which is not present in COS7 cells was revealed. In Table 3, the molecular weight of each expression product is shown.

Table 3

| HP Number | Supernatant of culture | Membrane fraction |
|-------------|------------------------|-------------------|
| | (kDa) | (kDa) |
| HP01263 | 50 | - |
| HP01299 | - | 30 |
| HP01526 | - | 22 |
| HP10230 | - | 24 |
| HP10408 | *** | 7 |
| HP10415 | - | 45 |
| HP10424 | - | 14 |
| HP10429 | - | 27 |
| HP10432 | - | 17 |
| HP10480 | - | 22 |

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(8) Clone Examples

<HP01263> (Sequence Number 1, 19, 37)

Determination of the whole base sequence for the cDNA insert of clone HP01263 obtained from the human liver cDNA 5 libraries revealed the structure consisting of a 5'-nontranslation region of 36 bp, an ORF of 1149 bp, and a 3'-nontranslation region of 316 bp. The ORF codes for a protein consisting of 382 amino acid residues with one transmembrane domain at the N-terminal. Figure 2 depicts the hydrophobicity 10 /hydrophilicity profile of the present protein obtained by the The in vitro translation resulted in Kyte-Doolittle method. formation of a translation product of 42 kDa, which is almost consistent with the molecular weight of 42,054 as predicted On expression in COS cells, an expression from the ORF. 15 product of about 50 kDa was observed in the culture supernatant. Therefore, said protein can be understood to be a secreted protein. Application of the rule (-3, -1) as a method for anticipation of a cutting site in a secretion signal sequence suggested that the mature protein would start from 20 methionine at 19 position.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human α -2-HS-glycoprotein (SWISS-PROT Accession No. P02765). Table 4 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human α -2-HS-glycoprotein (GP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the

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protein of the present invention. The both proteins possessed a homology of 25.5%. The cysteine position is reserved and this region is analogous to that in cystatins (thiol proteinase inhibitors). There are observed other analogy with histidine-rich glycoprotein (P04196, 30.9%/194 amino acid residues), kininogen (P01045, 24.1%/261 amino acid residues), tyrosine kinase inhibitor (A32827, 24.4%/291 amino acid residues), and so on.

Table 4

10 HP MGLLLPLALCILVLCCGAMSPPQLALNPSALLSR--GCNDSDVLAVAGFALRDINKDRKD .*.** * . ..*. * .*.*. .. * .*. *. GP MKSLVLLLCLAQLWGCHSAPHGPGLIYRQPNCDDPETEEAALVAIDYINQNLPW HP GYVLRLNRVNDAQEYRRGGLGSLFYLTLDVLETDCHVLRKKAWQDCGMRIFFE-SVYGQC 15 GP GYKHTLNQIDEVKVWPQQPSGELFEIEIDTLETTCHVLDPTPVARCSVRQLKEHAVEGDC HP K-AIFYMNNPSRVLYLAAYNCTLRPVSKKKIYMTCPDCPSSIPTDSSNHQVLEAATESLA GP DFQLLKLDGKFSVVY---AKCDSSPDSAEDVRKVCQDCPLLAPLN--DTRVVHAAKAALA 20 HP KYNNENTSKQYSLFKVTRASSQWVVGPSYFVEYLIKESPC---TKSQASSCSLQSSDSVP .*..*... * ...** . ** .**. * ...*.*.* ... GP AFNAQNNGSNFQLEEISRAQLV-PLPPSTYVEFTVSGTDCVAKEATEAAKCNLLAEKQY-HP VGLCKGSLTRTHWEKFVSVTCDFFESQAPATGSENSAVNQK-PTNLPKVEESQQKNTPPT *.**..*. . *.***. *..*. ** 25 GP -GFCKATLSEKLGGAEVAVTCTVFQTQPVTSQPQPEGANEAVPTPVVDPDAPPSPPLGAP HP DSPSKAGPRGSVQYLPDLDDKNSQEKGPQEAFPVHLDLTTNPQGETLDISFLFLEPMEEK . *. ..*..* *. GP GLPPAGSPPDSHVLLAAPPGHQLHRAHYDLRHTFMGVVSLGSPSGEVSHPRKTRTVVQPS HP LVVLPFPKEKARTAECPGPAQNASPLVLPP 30 GP VGAAAGPVVPPCPGRIRHFKV

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H57204), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention. Hereupon, most of ESTs matching with the present cDNA are available from liver cDNA libraries, whereby the present clone is considered to be expressed specifically in the liver.

The present protein, because of being a type-II membrane protein, is considered to exert its function as a receptor on the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. The present protein, because of bearing a cystatin-like domain, is considered to possess a proteinase-inhibitor activity as well as many physiological activities in the same manner as for other members of this family. In addition, the present protein, because of being expressed specifically in liver cells, is considered to play a significant role for maintaining the liver function.

<HP01299> (Sequence Number 2, 20, 38)

Determination of the whole base sequence for the cDNA insert of clone HP01299 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 110 bp, an ORF of 954 bp, and a 3'-non-translation region of 285 bp. The ORF codes for a protein consisting of 317 amino acid residues with two or more transmembrane domains. Figure 3 depicts the hydrophobicity/hydrophilicity profile of the present protein

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obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 32 kDa that was almost consistent with the molecular weight of 35,965 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the rat retinol dehydrogenase (NBRF Accession No. A55884). Table 5 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the rat retinol dehydrogenase (RN). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 65.3% among the entire regions.

Table 5

| | НР | ${\tt MWLYLAAFVGLYYLLHWYRERQVVSHLQDKYVFITGCDSGFGNLLARQLDARGLRVLAAC}$ |
|----|----|--|
| 5 | | **** *.**. **. **. ******************* |
| | RN | ${\tt MWLYLLALVGLWNLLRLFRERKVVSHLQDKYVFITGCDSGFGNLLARQLDRRGMRVLAAC}$ |
| | HP | ${\tt LTEKGAEQLRGQTSDRLETVTLDVTKMESIAAATQWVKEHVGDRGLWGLVNNAGILTPIT}$ |
| | | *************************************** |
| | RN | ${\tt LTEKGAEQLRSKTSDRLETVILDVTKTESIVAATQWVKERVGNRGLWGLVNNAGISVPVG}$ |
| 10 | HP | LCEWLNTEDSMNMLKVNLIGVIQVTLSMLPLVRRARGRIVNVSSILGRVAFFVGGYCVSK |
| | | ****.**.**.**.***.***.**.**.**.**. |
| | RN | PNEWMRKKDFASVLDVNLLGVIEVTLNMLPLVRKARGRVVNIASTMGRMSLVGGGYCISK |
| | HP | YGVEAFSDILRREIQHFGVKISIVEPGYFRTGMTNMTQSLERMKQSWKEAPKHIKETYGQ |
| | | ******* ******** *.******. ***.** |
| 15 | RN | YGVEAFSDSLRRELTYFGVKVAIIEPGGFKTNVTNMERLSDNLKKLWDQTTEEVKEIYGE |
| | HP | QYFDALYNIMKEGLLNCSTNLNLVTDCMEHALTSVHPRTRYSAGWDAKFFFIPLSYLPTS |
| | | * ****.******* ********** |
| | RN | KFQDSYMKAMESLVNTCSGDLSLVTDCMEHALTSCHPRTRYSPGWDAKFFYLPMSYLPTF |
| | HP | LADYILTRSWPKPAQAV |
| 20 | | *.* ***.*. |
| | RN | LSDAVIHWGSVKPARAL |

Furthermore, the search of GenBank using the base sequence
25 of the present cDNA revealed that there existed some ESTs
possessing the homology of 90% or more (for example, Accession
No. R35197), but any of them was shorter than the present cDNA
and did not contain the initiation codon.

The rat retinol dehydrogenase has been found as a 30 microsomal membrane protein participating in the retinoic acid

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biosynthesis in the liver [Chai, X. et al., J. Biol. Chem. 270: 28408-28412 (1995)]. Accordingly, its homologue, the protein of the present invention, is considered to possess a similar function and can be utilized for diagnosis and treatment of diseases caused by the abnormality of this protein.

<HP01347> (Sequence Number 3, 21, 39)

Determination of the whole base sequence for the cDNA insert of clone HP01347 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-10 translation region of 24 bp, an ORF of 891 bp, and a 3'-nontranslation region of 728 bp. The ORF codes for a protein consisting of 296 amino acid residues with one transmembrane N-terminal. Figure 4 domain at the depicts hydrophobicity/hydrophilicity profile of the present protein 15 obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified and the urokinase activity was detected on the membrane surface, upon transduction into the COS7 cells of an expression vector 20 in which a HindIII-SacI fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 73 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein is considered to be a type-II membrane protein. The in vitro 25 translation resulted in the formation of a translation product of 33 kDa that was almost consistent with the molecular weight of 33,527 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was

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analogous to the human HIV envelope glycoprotein gp120-binding C-type lectin (GenBank Accession No. M98457). Table 6 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human HIV envelope glycoprotein gp120-binding C-type lectin (CL). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 85.6% among 284 amino acid residues. There is observed at the downstream of the transmembrane domain a sequence with seven repetition of Ile-Tyr-Gln-Xaa-Leu-Thr-Xaa-Leu-Lys-Ala-Ala-Val-Gly-Glu-Leu-Xaa-Xaa-Xaa-Ser-Lys-Xaa-Gln-Xaa.

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Table 6

| | HP | MSDSKEPRVQQLGLLGCLGHGALVLQLLSFMLLAGVLVAI |
|----|----|--|
| | | ****** ***** **** |
| 5 | CL | MSDSKEPRLQQLGLLEEEQLRGLGFRQTRGYKSLAGCLGHGPLVLQLLSFTLLAGL |
| | HP | LVQVSKVPSSLSQEQSEQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE |
| | | ***************************** |
| | CL | LVQVSKVPSSISQEQSRQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE |
| | HP | KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRL |
| 10 | | ******************************* |
| | CL | KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTWLKAAVGELPEKSKMQEIYQELTRL |
| | HP | KAAVGELPEKSKLQEIYQELTELKAAVGELPEKSKLQEIYQELTQLKAAVGELPDQSKQQ |
| | | ******* **** ****** ******** ******* **** |
| | CL | KAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQ |
| 15 | HP | QIYQELTDLKTAFERLCRHCPKDWTFFQGNCYFMSNSQRNWHDSVTACQEVRAQLVVIKT |
| | | .*****.**.* ****** .***************** |
| | CL | EIYQELTQLKAAVERLCHPCPWEWTFFQGNCYFMSNSQRNWHDSITACKEVGAQLVVIKS |
| | HP | AEEQLPAVLEQWRTQQ |
| | | **** *. * |
| 20 | CL | AEEQNFLQLQSSRSNRFTWMGLSDLNQEGTWQWVDGSPLLPSFKQYWNRGEPNNVGEEDC |

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H90360), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The present protein, because of being a type-II membrane 30 protein, is considered to exert its function as a receptor on

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the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. Hereupon, the human HIV envelope glycoprotein gpl20-binding C-type lectin that is highly homologous with the present protein has been found as a CD4-independent HIV receptor [Curtis, B. M. et al., Proc. Natl. Acad. Sci. USA 89: 8356-8360 (1992)].

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<HP01440> (Sequence Number 4, 22, 40)

Determination of the whole base sequence for the cDNA insert of clone HP01440 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 37 bp, an ORF of 594 bp, and a 3'-non-translation region of 98 bp. The ORF codes for a protein consisting of 197 amino acid residues with four transmembrane domains. Figure 5 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 20,822 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human tumor-associated antigen L6 (SWISS-PROT Accession No. P30408). Table 7 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human tumor-associated antigen L6 (L6).

- represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

a homology of 47.0% among the entire regions.

Table 7

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. T55097), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

25 The human tumor-associated antigen L6 is a member of a membrane antigen TM4 superfamily proteins which are expressed in large quantities on the surface of human tumor cells [Marken, J. S. et al., Proc. Natl. Acad. Sci. USA 89: 3503-3507 (1992)]. Since these membrane antigens are expressed 30 specifically on some specified cells or cancer cells,

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antibodies against these antigens, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are expressed are applicable for detection of the corresponding ligands and so on.

<HP01526> (Sequence Number 5, 23, 41)

Determination of the whole base sequence for the cDNA insert of clone HP01526 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 83 bp, an ORF of 666 bp, and a 3'-non-translation region of 573 bp. The ORF codes for a protein consisting of 221 amino acid residues with a hydrophobic region of putative six transmembrane domains. Figure 6 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was almost consistent with the molecular weight of 25,030 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the mouse interstitial cell protein (GenBank Accession No. X96618). Table 8 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the mouse interstitial cell protein (MM). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

a homology of 79.6% among the entire regions.

Table 8

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. H02682), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

25 The mouse interstitial cell protein has been cloned as a membrane protein that is expressed with highly increasing in interstitial cells stimulated by a cytokine [Tagoh, H. et al., Biochem. Biophys. Res. Commun. 221: 744-749 (1996)]. Since these membrane proteins are expressed specifically on some 30 specified cells and cancer cells, antibodies against these

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proteins, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are expressed are applicable for detection of the corresponding ligands and so on.

<HP10230> (Sequence Number 6, 24, 42)

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Determination of the whole base sequence for the cDNA insert of clone HP10230 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 190 bp, an ORF of 756 bp, and a 3'-nontranslation region of 2099 bp. The ORF codes for a protein consisting of 251 amino acid residues with at least one transmembrane domain. Figure 7 depicts hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 30 kDa that was almost consistent with the molecular weight of 28,800 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein F25D7.1 (GenBank Accession No. Z78418). Table 9 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein F25D7.1 (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 49.8% among the entire regions.

40

Table 9

HS MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFL-WPEAFLYRFQIWRPITAT 5 CE MDLENFLLGIPIVTRYWFLASTIIPLLGRFGFINVQWMFLQW-DLVVNKFQFWRPLTAL HS FYFPVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNW-ICIVITGLAMDM CE IYYPVTPQTGFHWLMMCYFLYNYSKALESETYRGRSADYLFMLIFNWFFCSGLC-MALDI HS QLLMIPLIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIGGSVINELIGNL 10 .*. *...***** *.*.* ****** ** * *****. *** .. *. .***.* CE YFLLEPMVISVLYVWCQVNKDTIVSFWFGMRFPARYLPWVLWGFNAVLRGGGTNELVGIL HS VGHLYFFLMFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGG CE VGHAYFFVALKYPDEYGV-DLISTPEFLHRLIPDEDGGIHG---QDGNIRGARQQPRG--15 HS RHNW--GQGFRLGDQ * * * * *** CE -HQWPGGVGARLGGN

20 Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. W01493), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10389> (Sequence Number 7, 25, 43)

Determination of the whole base sequence for the cDNA insert of clone HP10389 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 62 bp, an ORF of

321 bp, and a 3'-non-translation region of 270 bp. The ORF codes for a protein consisting of 106 amino acid residues with a hydrophobic region of putative two transmembrane domains. Figure 8 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 12 kDa that was almost consistent with the molecular weight of 11,528 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any of known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H70816), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10408> (Sequence Number 8, 26, 44)

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Determination of the whole base sequence for the cDNA insert of clone HP10408 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 74 bp, an ORF of 237 bp, and a 3'-non-translation region of 128 bp. The ORF codes for a protein consisting of 78 amino acid residues with a putative signal sequence at the N-terminal as well as a sequence of one putative interior transmembrane domain. Figure 9 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified

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upon transduction into the COS7 cells of an expression vector in which a HindIII-BglII fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 70 amino acid residues in the present protein was inserted at the 5 HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 9 kDa that was almost consistent with the molecular weight of 8,396 predicted from the ORF.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T94049), but they were shorter than the present cDNA and molecule containing the initiation codon was not identified.

<HP10412> (Sequence Number 9, 27, 45) 15

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Determination of the whole base sequence for the cDNA insert of clone HP10412 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 55 bp, an ORF of 945 bp, and a 3'-non-20 translation region of 131 bp. The ORF codes for a protein consisting of 314 amino acid residues with one transmembrane depicts the N-terminal. 10 Figure domain at the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-ApaI fragment (treated with mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 65

43

amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 44 kDa that was somewhat larger than the molecular weight of 35,610 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein of 28.5 kDa (SWISS-PROT Accession No. P34623). Table 10 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein of 28.5 kDa (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 42.8% in the C-terminal region of 243 amino acid residues.

Table 10

HP MVAPVWYLVAAALLVGFILFLTRSRGRAASAGQEPLHNEELAGAGRVAQPGPLEPEEPRA 5 GGRPRRRDLGSRLQAQRRAQRVAWAEA--DENEEEAVILAQEEEGVEKPAETHLSGKIG CE MRRNARRRVNRDEO EDGFVNHMMNDGEDVEDLDGGAEO FEYDEDGKKIG HP AKKLRKLEEKQARKAQREAEEAEREERKRLESQREAEWKKEEERLRLEEEQKEEEE--RK * **..*... ** * ****** *..* * *..*** . *...*.** CE KRKAAKLQAKEEKRQMREYEVREREERKRREEER--EKKRDEERAKEEADEKAEEERLRK HP AREEQAQREHEEYLKLKEAFVVEEEGVGETMTEEQSQSFLTEFINYIKQSKVVLLEDLAS CE EREEKERKEHEEYLAMKASFAIEEEG-TDAIEGEEAENLIRDFVDYVKTNKVVNIDELSS HP QVGLRTQDTINRIQDLLAEGTITGVIDDRGKFIYITPEELAAVANFIRQRGRVSIAELAQ 15 CE HFGLKSEDAVNRLQHFIEEGLVQGVMDDRGKFIYISDEEFAAVAKFINQRGRVSIHEIAE HP ASNSLIAWGRESPAQAPA .**.** . *.*. CE QSNRLIRLETPSAAE 20

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T09311), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10413> (Sequence Number 10, 28, 46)

Determination of the whole base sequence for the cDNA 30 insert of clone HP10413 obtained from the human stomach cancer

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cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 78 bp, an ORF of 588 bp, and a 3'-nontranslation region of 1209 bp. The ORF codes for a protein consisting of 195 amino acid residues with one transmembrane Figure domain the N-terminal. 11 depicts hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-PmaCI fragment containing a cDNA fragment encoding the N-terminal 65 amino acid residues in the present protein was inserted at the HindIII-PmaCI site of pSSD3. The in vitro translation resulted in the formation of a translation 15 product of 28 kDa that was somewhat larger than the molecular weight of 21,671 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the swine steroidal membrane-binding protein (GenBank Accession No. X99714). Table 11 indicates comparison of the amino acid sequences between the human protein of the present invention (HP) and the swine steroidal membrane-binding protein (SS). - represents a gap, * represents an amino acid residue identical to that in the protein of the 25 present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 96.4% among the entire regions.

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Table 11

| | нР | MAAEDVVATGADPSDLESGGLLHEIFTSPLNLLLLGLCIFLLYKIVRGDQPAASGDSDDD |
|----|----|--|
| | | ************ |
| 5 | SS | MAAEDVAATGADPSELEGGGLLHEIFTSPLNLLLLGLCIFLLYKIVRGDQPAAS-DSDDD |
| | HP | EPPPLPRLKRRDFTPAELRRFDGVQDPRILMAINGKVFDVTKGRKFYGPEGPYGVFAGRD |
| | | ************ |
| | SS | EPPPLPRLKRRDFTPAELRRFDGVQDPRILMAINGKVFDVTKGRKFYGPEGPYGVFAGRD |
| • | HP | ASRGLATFCLDKEALKDEYDDLSDLTAAQQETLSDWESQFTFKYHHVGKLLKEGEEPTVY |
| LO | | ************ |
| | SS | ASRGLATFCLDKEALKDEYDDLSDLTPAQQETLNDWDSQFTFKYHHVGKLLKEGEEPTVY |
| | HP | SDEEEPKDESARKND |
| | • | ****** |
| | SS | SDEEEPKDESARKND |
| 15 | | |

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA021062), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10415> (Sequence Number 11, 29, 47)

Determination of the whole base sequence for the cDNA insert of clone HP10415 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 71 bp, an ORF of 1389 bp, and a 3'-non-translation region of 103 bp. The ORF codes for a protein consisting of 462 amino acid residues with one transmembrane domain at the N-terminal. Figure 12 depicts the hydrophobicity/hydrophilicity profile of the present protein

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 48 kDa that was somewhat smaller than the molecular weight of 52,458 predicted from the ORF.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the cytochrome P450 as exemplified by the simian cytochrome P450IIIA8 (SWISS-PROT Accession No. P33268). Table 12 indicates the comparison of the amino acid sequences between 10 the human protein of the present invention (HP) and the simian cytochrome P450IIIA8 (CP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The 15 both proteins possessed a homology of 21.3% among the entire regions.

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Table 12

| | HP | MLDFAIFAVTFLLALVGAVLYLYPASRQAAGIPGITPTEEKDGNLPDIVN-SGSLHEF |
|----|-----|--|
| | | .******* |
| 5 | CP | MDLIPDLAVETWLLLAVTLVLLYLYGTHSHGLFKKLGIPGPTPLPLLGNILSYRKGFWTF |
| | HP | LVNLHERYGPVVSFWFGRRLVVSLGTVDVLKQHINPNKTLDPFETMLK-SLLRYQSGGGS |
| | | ** * .*. **. * * * * |
| | CP | DMECYKKYGKVWGFYDGRQPVLAITDPNMIK-TVLVKECYSVFTNRRPFGPVGFMKNAIS |
| | HP | VSENHMRKKLYENGVTDSLKSNFALLLKLSEELLDKWLSYPET-QHVPLSQHMLGF |
| 10 | | **. *** * * |
| | CP | IAEDEEWKRIRSLLSPTFTSGKLKEMVPIIAKYGDVLVRNLRREAETGKPVTLKDVFGAY |
| | HP- | AMKSVTQMVMGSTF-EDDQEVIRFQKNHGTVWSEIGKGFLDGSLDKNM |
| | | .** .*** *. *. * |
| | ÇP | SMDVITSTSFGVNIDSLNNPQDPFVENTKKLLRFDFLDPFFLSITIFPFIIPILEVLNIS |
| 15 | HP | TRKKQYEDALMQ-LESVLRNIIKE-RKGR-NFSQHIFIDSLVQGNLNDQQILEDS |
| | | |
| | CP | ${\tt IFPREVTSFLRKSVKRIKESRLKDTQKHRVDFLQLMIDSQNSKETESHKALSDLELVAQS}$ |
| | HP | MIFSLASCIITAKLCTWAICFLTTSEEVQKKLYEEINQVF-GNGPVTPEKIEQLRYCQHV |
| | | .** .* |
| 20 | CP | IIFIFAGYETTSSVLSFIIYELATHPDVQQKLQEEIDTVLPNKAPPTYDTVLQMEYLDMV |
| | HP | ${\tt LCETVRTAKLTPVSAQLQDIEGKIDRFIIPRETLVLYALGVVLQDPNTWPSPHKFDPDRF}$ |
| | | . **.* |
| | HP | VNETLRIFPIAM RLERVCKKDVEINGIFIPKGVVVMIPSYALHHDPKYWPEPEKFLPERF |
| | HP | $\hbox{\ttDDELVMKTFSSLGFSGTQECPELRFAYMVTTVLLSVLVKRLHLLSVEGQVIETKYE}$ |
| 25 | | .** ****** * * * |
| | CP | ${\tt SKKNNDNIDPYIYTPFG-SGPRNCIGMRFALMNMKLAIIRVLQNFSFKPCKETQIPLKLR}$ |
| | HP | LVTSSREEAWITVSKRY |
| | | * |
| | CP | LGGLLQTEKPIVLKIESRDGTVSGA |
| | | |

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs

possessing the homology of 90% or more (for example, Accession No. AA381169), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The cytochrome P450 participates in the drug metabolism and can be utilized as a catalyst in organic synthesis reactions such as oxidation and so on.

<HP10419> (Sequence Number 12, 30, 48)

Determination of the whole base sequence for the cDNA 10 insert of clone HP10419 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 170 bp, an ORF of 744 bp, and a 3'-nontranslation region of 1116 bp. The ORF codes for a protein consisting of 247 amino acid residues with a hydrophobic region 15 of putative seven transmembrane domains. Figure 13 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing 20 the homology of 90% or more (for example, Accession No. AA340663), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10424> (Sequence Number 13, 31, 49)

Determination of the whole base sequence for the cDNA 25 insert of clone HP10424 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 97 bp, an ORF of 342 bp, and a 3'-nontranslation region of 54 bp. The ORF codes for a protein

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consisting of 113 amino acid residues with one transmembrane Figure 14 depicts the N-terminal. domain hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that 5 the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-AccI fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 58 amino 10 acid residues in the present protein was inserted at the HindIII-SmaI site of pSSD3. The in vitro translation resulted in the formation of a translation product of 14 kDa that was somewhat larger than the molecular weight of 12,784 predicted from the ORF.

of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA401979), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10428> (Sequence Number 14, 32, 50)

Determination of the whole base sequence for the cDNA insert of clone HP10428 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 287 bp, an ORF of 1098 bp, and a 3'-non-translation region of 659 bp. The ORF codes for a protein consisting of 365 amino acid residues with a hydrophobic region of putative nine transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile of

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the present protein obtained by the Kyte-Doolittle method. The result of the in vitro translation did not reveal the formation of distinct bands and only revealed the formation of smeary bands at the high-molecular-weight position.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the baker's yeast hypothetical membrane protein YML038c (NBRF Accession No. S49741). Table 13 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the baker's yeast hypothetical membrane protein YML038c (SC). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 26.3% among the N-terminal region of 281 amino acid residues.

Table 13

| | - | |
|----|----|--|
| | HP | MGRWALDVAFLWKAVLTLGLVL-LYYCFSIGITFYNKWLTKSFHFPLFMTMLHLA |
| | | **. *.* ***.*. |
| 5 | sc | MNRTVFLAFVFGWYFCS-IALSIYNRWMFDPKDGLGIGYPVLVTTFHQA |
| | HP | VIFLFSALSRALVQCSSHRARVVLSWADYLRRVAPTALATALDVGLSNWSFLYVTVS |
| | | *.*. * |
| | sc | TLWLLSGIYIKLRHKPVKNVLRKNNGFNWSFFLKFLLPTAVASAGDIGLSNVSFQYVPLT |
| | HP | LYTMTKSSAVLFILIFSLIFKLEELRAALVLVVLLIAGGLFMFTYKSTQ-FN |
| LO | | .**** *.*.* |
| | sc | IYTIIKSSSIAFVLLFGCIFKLEKFHWKLALSVIIMFVGVALMVFKPSDSTSTKNDQALV |
| | нР | VEGFALVLGASFIGGIRWTLTQMLLQKAELGLQNPIDTMFHLQPLMFLGLFPLFAVFEGL |
| • | | * ***.**.**. *** |
| | sc | IFGSFLVLASSCLSGLRWVYTQLMLRNNPIQTNTAAAVEES-DGALFTENEDNVDNEPVV |
| 15 | HP | HLSTSEKIFRFQDT-GLLLRVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEV |
| | | .* * *. * * * *** * *** |
| | sc | NLANNKMLENFGESKPHPIHTIHQLAPIMGITLLLTS-LLVEKPFPGIFS-SSIFRLD |
| | HP | CTLLLAAHLLGDQISLLNWLGFALCLSGISLHVALKALHSRGDGGPKALKGLGSSPDLEL |
| | | |
| 20 | sc | TSNGGVGTETTVLSIVRGIVLLILPGFAVFLLTICEFSILEQTPVLTVSIVGIVKELLTV |
| | НР | LLRSSQREEGDNEEEEYFVAQGQQ |
| | | |
| | sc | IFGIIILSERLSGFYNWLGMLIIMADVCYYNYFRYKQDLLQKYHSVSTQDNRNELKGFQD |
| | | |

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Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA018345), but it can not be assessed whether these ESTs

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with partial sequences code for the same protein as the protein of the present invention.

<HP10429> (Sequence Number 15, 33, 51)

Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 156 bp, an ORF of 681 bp, and a 3'-nontranslation region of 206 bp. The ORF codes for a protein consisting of 226 amino acid residues with four transmembrane 10 domains. Figure 16 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 25 kDa that was almost consistent with the molecular weight of 25,321 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or 20 more (for example, Accession No. AA315933), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10432> (Sequence Number 16, 34, 52)

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Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human liver cDNA 25 libraries revealed the structure consisting of a 5'-nontranslation region of 28 bp, an ORF of 390 bp, and a 3'-nontranslation region of 554 bp. The ORF codes for a protein consisting of 129 amino acid residues with a signal-like sequence at the N-terminal and one interior transmembrane domain. Therefore, the present protein is considered to be a type-I membrane protein. Figure 17 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T74424), but the same ORF as that in the present cDNA was not identified.

<HP10433> (Sequence Number 17, 35, 53)

Determination of the whole base sequence for the cDNA insert of clone HP10433 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 72 bp, an ORF of 492 bp, and a 3'-nontranslation region of 131 bp. The ORF codes for a protein consisting of 163 amino acid residues with one transmembrane 20 domain the N-terminal. Figure 18 depicts the at hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified 25 upon transduction into the COS7 cells of an expression vector in which a HindIII-Eco81I fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 137 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein WO 98/55508

is considered to be a type-II membrane protein. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 18,617 predicted from the ORF.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or 10 more (for example, Accession No. H84693), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

<HP10480> (Sequence Number 18, 36, 54)

Determination of the whole base sequence for the cDNA insert of clone HP10480 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 79 bp, an ORF of 582 bp, and a 3'-non-translation region of 1253 bp. The ORF codes for a protein consisting of 193 amino acid residues with four transmembrane domains. Figure 19 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 21,445 predicted from the ORF.

25 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or

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more (for example, Accession No. W93606), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

The present invention provides human proteins having transmembrane domains and cDNAs encoding said proteins. All of the proteins of the present invention are putative proteins controlling the proliferation and differentiation of the cells, because said proteins exist on the cell membrane. Therefore, the proteins of the present invention can be used as 10 pharmaceuticals or as antigens for preparing antibodies against said proteins. Furthermore, said DNAs can be used for the expression of large amounts of said proteins. The cells expressing large amounts of membrane proteins with transfection of these membrane protein genes can be applied to the detection 15 of the corresponding ligands, the screening of novel low-molecular medicines, and so on.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for

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analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA 10 sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known the process of discovering other polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for 15 examination of expression patterns; to raise anti-protein antibodiesusing DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in 20 a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in

assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of 15 being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A 20 Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

25 <u>Nutritional Uses</u>

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source

and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation

10 Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

25 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H.

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Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Po lyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

differentiation proliferation and Assays for include, without hematopoietic and lymphopoietic cells 20 limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 25 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 -Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et

al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986;
Measurement of human Interleukin 11 - Bennett, F., Giannotti,
J., Clark, S.C. and Turner, K. J. In Current Protocols in
Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley
and Sons, Toronto. 1991; Measurement of mouse and human
Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and
Turner, K.J. In Current Protocols in Immunology. J.E.e.a.
Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto.
1991.

10 Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); 20 Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined

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immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial orfungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein 15 of the present invention include, for example, connective multiple sclerosis, systemic tissue disease, erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, 20 insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or 25 other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be

possible to immune responses, in a number of ways. regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing The functions of the induction of an immune response. 5 activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, 10 which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure 15 to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in 20 graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in Typically, in tissue transplants, tissue transplantation. rejection of the transplant is initiated through its 25 recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2

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activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen

(e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the

corresponding costimulatory signal. Blocking B lymphocyte

antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an

immunosuppressant. Moreover, the lack of costimulation may

also be sufficient to anergize the T cells, thereby inducing

tolerance in a subject. Induction of long-term tolerance by B

lymphocyte antigen-blocking reagents may avoid the necessity of

repeated administration of these blocking reagents. To achieve

sufficient immunosuppression or tolerance in a subject, it may

15 also be necessary to block the function of a combination of B

lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

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Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the 5 production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor: ligand interactions of B lymphocyte 10 antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. 15 The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid 20 mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B

lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression

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vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface 10 of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II 15 molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_2 microglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins 20 on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which 25 blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a

T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

5 Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 20 Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that 25 affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John

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Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Thl and CTL responses) include, without limitation, those 5 described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in 10 Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those 15 described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 20 182:255-260, 1995; Nair et al., Journal Virology of 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in:

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Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in 15 regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation 20 of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the 25 growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently

of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation 5 of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal 10 nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo (i.e., bone or ex-vivo in conjunction with marrow progenitor transplantation or with peripheral cell transplantation (homologous or heterologous)) as normal cells 15 or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney,

M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high 5 proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area assay, Ploemacher, R.E. Culture forming cell In Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., 15 New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

- A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.
- A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the

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invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue

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formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendonligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of 10 tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

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The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as 20 mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral peripheral neuropathy localized nerve injuries, and neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders,

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such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International WO95/16035 cartilage, tendon); Publication No. (bone, Patent Publication No. WO95/05846 International 5 neuronal); International Patent Publication No. W091/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year 10 Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

A protein of the present invention may also exhibit inhibin-related activities. Inhibins activinor 15 characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of 20 the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, 25 as a homodimer or as a heterodimer with other protein subunits of the inhibin- β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of

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the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

5 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell

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population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis)consist of assays

10 that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in

15 Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (includinghereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A

protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system 5 vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate 15 activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). 25 Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments receptors and ligands) may themselves be useful as inhibitors

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of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include

5 without limitation those described in:Current Protocols in
Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies,
E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and
Wiley-Interscience (Chapter 7.28, Measurement of Cellular
Adhesion under static conditions 7.28.1-7.28.22), Takai et al.,

10 Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al.,
J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp.
Med. 169:149-160 1989; Stoltenborg et al., J. Immunol.
Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

Proteins of the present invention may also exhibit 15 anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by 20 inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can 25 be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis,

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complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of ytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

20 Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in

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bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, 5 protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent 10 behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related 15 diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another 20 material or entity which is cross-reactive with such protein.

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Sequence Table

| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 1: | | | | | | | |
|----|-----|-----|------|------|------|------|-------------|------|------|-------|-----|-----|-----|-----|-----|-----|
| 5 | | (| i) S | EQUE | NCE | CHAR | ACTE | RIST | ics: | | | | | | | |
| | | | | (A) | LEN | GTH: | 382 | | | | | | | | | |
| | | | | (B) | TYP | E: A | mino | aci | d | | | | | | | |
| | | | | (D) | TOP | OLOG | Y: L | inea | r | | | | | | | |
| | | (| ii) | SEQU | ENCE | KIN | D: P | rote | in | | | | | | | |
| 10 | | (| iii) | HYP | OTHE | TICA | L: N | 0 | | | | | | | | |
| | | | | | | | | | | | | | | | • | |
| | | (| vi) | ORIG | INAL | sou | RCE: | • | | | | | | | | |
| | | | | (A) | ORG | ANIS | M: <i>H</i> | omo | sapi | ens . | | | | | | |
| | | | | (B) | CEL | L KI | ND: | Live | r | | | | | | | |
| 15 | | | | (D) | CLO | NE N | AME: | HPO: | 1263 | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | | (: | xi) | SEQU | ENCE | DES | CRIP | TION | : SE | Q ID | NO: | 1: | | | | |
| | | | | | | | | | | | | | | | | |
| | Met | Gly | Leu | Leu | Leu | Pro | Leu | Ala | Leu | Cys | Ile | Leu | Val | Leu | Cys | Сув |
| 20 | 1 | | | | 5 | | | | | 10 | | | | | 15 | • |
| | Gly | Ala | Met | Ser | Pro | Pro | Gln | Leu | Ala | Leu | Asn | Pro | Ser | Ala | Leu | Leu |
| | | | | 20 | | | | | 25 | | | | | 30 | | |
| | Ser | Arg | Gly | Cys | Asn | Asp | Ser | Asp | Val | Leu | Ala | Val | Ala | Gly | Phe | Ala |
| | | | 35 | | | | | 40 | | | | | 45 | | | |
| 25 | Leu | Arg | Asp | Ile | Asn | Lys | Asp | Arg | Lys | Asp | Gly | Tyr | Val | Leu | Arg | Leu |
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| | Asn | Arg | Val | Asn | Asp | Ala | Gln | Glu | Tyr | Arg | Arg | Gly | Gly | Leu | Gly | Ser |
| | 65 | | ٠ | | | 70 | • . | | | | 75 | | | | | 80 |
| | Leu | Phe | Tyr | Leu | Thr | Leu | Asp | Val | Leu | G1u | Thr | Asp | Cys | His | Val | Leu |
| 30 | | | | | 85 | | | | | 90 | | | | | 95 | |
| | Arg | Lys | Lys | Ala | Trp | Gln | Asp | Cys | Gly | Met | Arg | Ile | Phe | Phe | Glu | Ser |
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| • | Val | Tyr | Gly | Gln | Cys | Lys | Ala | Ile | Phe | Tyr | Met | Asn | Asn | Pro | Ser | Arg |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| 35 | Val | Leu | Tyr | Leu | Ala | Ala | Tyr | Asn | Cys | Thr | Leu | Arg | Pro | Val | Ser | Lys |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| | Lys | Lys | Ile | Tyr | Met | Thr | Cys | Pro | Asp | Cys | Pro | Ser | Ser | Ile | Pro | Thr |

| | Asp | Ser | Ser | Asn | His | G1n | Val | Leu | Glu | Ala | Ala | Thr | Glu | Ser | Leu | A1 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | | | 165 | | | | | 170 |) | • | | | 175 | |
| | Lys | Tyr | Asn | Asn | Glu | Asn | Thr | Ser | Lys | Gln | Tyr | Ser | Leu | Phe | Lys | Va] |
| | | | | 180 | | | | | 185 | | | | | 190 | | |
| 5 | Thr | Arg | Ala | Ser | Ser | Gln | Trp | Val | Val | Gly | Pro | Ser | Tyr | Phe | Va1 | Gli |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| | Tyr | Leu | I1e | Lys | Glu | Ser | Pro | Cys | Thr | Lys | Ser | Gln | Ala | Ser | Ser | Cys |
| | • | 210 | | | | | 215 | | | | | 220 | | | | |
| | Ser | Leu | Gln | Ser | Ser | Asp | Ser | Val | Pro | Val | Gly | Leu | Cys | Lys | Gly | Ser |
| 10 | 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| | Leu | Thr | Arg | Thr | His | Trp | Glu | Lys | Phe | Val | Ser | Val | Thr | Cys | Asp | Phe |
| | • | | | | 245 | | , | | | 250 | | | | | 255 | |
| | Phe | Glu | Ser | Gln | Ala | Pro | Ala | Thr | Gly | Ser | Glu | Asn | Ser | Ala | Val | Asn |
| | | | | 260 | | | | | 265 | | | | | 270 | | |
| 15 | Gln | Lys | Pro | Thr | Asn | Leu | Pro | Lys | Val | Glu | Glu | Ser | Gln | G1n | Lys | Asn |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| | Thr | | Pro | Thr | Asp | Ser | Pro | Ser | Lys | Ala | Gly | Pro | Arg | Gly | Ser | Va1 |
| | | 290 | | | | | 295 | | | | | 300 | | | | |
| | | Tyr | Leu | Pro | Asp | Leu | Asp | Asp | Lys | Asn | Ser | Gln | Glu | Lys | Gly | Pro |
| 20 | 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| | Gln | Glu | Ala | Phe | | Val | His | Leu | Asp | Leu | Thr | Thr | Asn | Pro | Gln | Gly |
| | | | | | 325 | | | | | 330 | | | | | 335 | |
| | Glu | Thr | Leu | Asp | Ile | Ser | Phe | Leu | Phe | Leu | Glu | Pro | Met | Glu | Glu | Lys |
| | | | | 340 | | | | | 345 | | | | | 350 | | |
| 25 | Leu | Val | | Leu | Pro | Phe | Pro | | Glu | Lys | Ala | Arg | Thr | Ala | Glu | Cys |
| | _ | | 355 | | | | | 360 | | | | | 365 | | | |
| | Pro | | Pro | Ala | Gln | Asn | | Ser | Pro | Leu | Val | Leu | Pro | Pro | | |
| | • | 370 | | | | | 375 | | | | | 380 | | | | |
| 2.0 | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |

- (2) INFORMATION FOR SEQ ID NO: 2:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 317
 - (B) TYPE: Amino acid
- 35 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No

85

| (vi) | ORIGINAL | SOURCE: |
|------|----------|---------|
|------|----------|---------|

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Liver

(D) CLONE NAME: HP01299

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Trp Leu Tyr Leu Ala Ala Phe Val Gly Leu Tyr Tyr Leu Leu His 10 Trp Tyr Arg Glu Arg Gln Val Val Ser His Leu Gln Asp Lys Tyr Val 25 30 Phe Ile Thr Gly Cys Asp Ser Gly Phe Gly Asn Leu Leu Ala Arg Gln 40 Leu Asp Ala Arg Gly Leu Arg Val Leu Ala Ala Cys Leu Thr Glu Lys 15 50 60 Gly Ala Glu Gln Leu Arg Gly Gln Thr Ser Asp Arg Leu Glu Thr Val 70 75 Thr Leu Asp Val Thr Lys Met Glu Ser Ile Ala Ala Ala Thr Gln Trp 90 -20 Val Lys Glu His Val Gly Asp Arg Gly Leu Trp Gly Leu Val Asn Asn 100 105 Ala Gly Ile Leu Thr Pro Ile Thr Leu Cys Glu Trp Leu Asn Thr Glu 120 Asp Ser Met Asn Met Leu Lys Val Asn Leu Ile Gly Val Ile Gln Val 25 130 135 140 Thr Leu Ser Met Leu Pro Leu Val Arg Arg Ala Arg Gly Arg Ile Val 150 155 Asn Val Ser Ser Ile Leu Gly Arg Val Ala Phe Phe Val Gly Gly Tyr 165 170 30 Cys Val Ser Lys Tyr Gly Val Glu Ala Phe Ser Asp Ile Leu Arg Arg 185 Glu Ile Gln His Phe Gly Val Lys Ile Ser Ile Val Glu Pro Gly Tyr 195 200 Phe Arg Thr Gly Met Thr Asn Met Thr Gln Ser Leu Glu Arg Met Lys 35 215 Gln Ser Trp Lys Glu Ala Pro Lys His Ile Lys Glu Thr Tyr Gly Gln 230 235 Gln Tyr Phe Asp Ala Leu Tyr Asn Ile Met Lys Glu Gly Leu Leu Asn

86 245 250 255 Cys Ser Thr Asn Leu Asn Leu Val Thr Asp Cys Met Glu His Ala Leu 260 265 270 Thr Ser Val His Pro Arg Thr Arg Tyr Ser Ala Gly Trp Asp Ala Lys 280 Phe Phe Phe Ile Pro Leu Ser Tyr Leu Pro Thr Ser Leu Ala Asp Tyr 290 295 300 Ile Leu Thr Arg Ser Trp Pro Lys Pro Ala Gln Ala Val 305 310 315 10 (2) INFORMATION FOR SEQ ID NO: 3: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 296 15 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Liver (D) CLONE NAME: HP01347 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Met Ser Asp Ser Lys Glu Pro Arg Val Gln Gln Leu Gly Leu Leu Gly 10 Cys Leu Gly His Gly Ala Leu Val Leu Gln Leu Leu Ser Phe Met Leu 30 20 25 30 Leu Ala Gly Val Leu Val Ala Ile Leu Val Gln Val Ser Lys Val Pro Ser Ser Leu Ser Gln Glu Gln Ser Glu Gln Asp Ala Ile Tyr Gln Asn 50 55 35 Leu Thr Gln Leu Lys Ala Ala Val Gly Glu Leu Ser Glu Lys Ser Lys 65 70 Leu Gln Glu Ile Tyr Gln Glu Leu Thr Gln Leu Lys Ala Ala Val Gly 85 90

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| | Glu | Leu | Pro | Glu | Lys | Ser | Lys | Leu | Gln | Glu | Ile | Tyr | Gln | Glu | Leu | Thr |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| | Arg | Leu | Lys | Ala | Ala | Val | Gly | Glu | Leu | Pro | Glu | Lys | Ser | Lys | Leu | Gln |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| 5 | Glu | Ile | Tyr | Gln | Glu | Leu | Thr | Arg | Leu | Lys | Ala | Ala | Val | Gly | Glu | Leu |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| | Pro | Glu | Lys | Ser | Lys | Leu | Gln | Glu | Ile | Tyr | Gln | Glu | Leu | Thr | Arg | Leu |
| | 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| | Lys | Ala | Ala | Val | Gly | Glu | Leu | Pro | Glu | Lys | Ser | Lys | Leu | Gln | Glu | Ile |
| 10 | | | | | 165 | | | | | 170 | | | | | 175 | |
| | Tyr | Gln | Glu | Leu | Thr | Glu | Leu | Lys | Ala | Ala | Val | Gly | Glu | Leu | Pro | G1u |
| | | | | 180 | | | | | 185 | | | | | 190 | • | |
| | Lys | Ser | Lys | Leu | Gln | Glu | Ile | Tyr | Gln | Glu | Leu | Thr | Gln | Leu | Lys | Ala |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| 15 | Ala | Val | Gly | Glu | Leu | Pro | Asp | Gln | Ser | Lys | Gln | Gln | Gln | Ile | Tyr | Gln |
| | | 210 | | | | | 215 | | | | | 220 | | | | |
| | Glu | Leu | Thr | Asp | Leu | Lys | Thr | Ala | Phe | Glu | Arg | Leu | Cys | Arg | His | Cys |
| | 225 | | | | | 230 | | | | • | 235 | | | | | 240 |
| | Pro | Lys | Asp | Trp | Thr | Phe | Phe | Gln | Gly | Asn | Cys | Tyr | Phe | Met | Ser | Asn |
| 20 | | | | | 245 | | | | | 250 | | | | | 255 | |
| | Ser | Gln | Arg | Asn | Trp | His | Asp | Ser | Val | Thr | Ala | Cys | Gln | Glu | Val | Arg |
| | | | | 260 | | | | | 265 | | | | | 270 | | |
| | Ala | Gln | | Val | Val | Ile | Lys | | Ala | Glu | Glu | Gln | Leu | Pro | Ala | Val |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| 25 | Leu | | G1n | Trp | Arg | Thr | | Gln | | | | | | | | |
| | | 290 | • | | | | 295 | | | | | | | • | | |
| | | | | | | | | | | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 4:

30 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 197
- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: Protein
- 35 (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

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| (B) | CELL | KIND: | Stomach | cancer |
|-----|------|-------|---------|--------|
| | | | | |

(D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

5 Met Cys Thr Gly Lys Cys Ala Arg Cys Val Gly Leu Ser Leu Ile Thr 1 5 15 Leu Cys Leu Val Cys Ile Val Ala Asn Ala Leu Leu Val Pro Asn 20 25 10 Gly Glu Thr Ser Trp Thr Asn Thr Asn His Leu Ser Leu Gln Val Trp 35 40 45 Leu Met Gly Gly Phe Ile Gly Gly Leu Met Val Leu Cys Pro Gly 55 Ile Ala Ala Val Arg Ala Gly Gly Lys Gly Cys Cys Gly Ala Gly Cys 15 75 Cys Gly Asn Arg Cys Arg Met Leu Arg Ser Val Phe Ser Ser Ala Phe 85 90 Gly Val Leu Gly Ala Ile Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu 105 20 Arg Asn Gly Pro Arg Cys Leu Met Asn Gly Glu Trp Gly Tyr His Phe 115 125 120 Glu Asp Thr Ala Gly Ala Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg 135 Cys Glu Ala Pro Pro Arg Val Val Pro Trp Asn Val Thr Leu Phe Ser 25 145 150 155 Leu Leu Val Ala Ala Ser Cys Leu Glu Ile Val Leu Cys Gly Ile Gln 165 170 Leu Val Asn Ala Thr Ile Gly Val Phe Cys Gly Asp Cys Arg Lys Lys

185

190

30 Gln Asp Thr Pro His

195

(2) INFORMATION FOR SEQ ID NO: 5:

- (1) SEQUENCE CHARACTERISTICS:
- 35 (A) LENGTH: 221
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 5 (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP01526

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

| 10 | Met | Glu | Ala | Gly | Gly | Phe | Leu | Asp | Ser | Leu | Ile | Tyr | Gly | Ala | Cys | Val |
|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| | Val | Phe | Thr | Leu | Gly | Met | Phe | Ser | Ala | Gly | Leu | Ser | Asp | Leu | Arg | His |
| | | | | 20 | | | | | 25 | | | | | 30 | | |
| | Met | Arg | Met | Thr | Arg | Ser | Val | Asp | Asn | Val | Gln | Phe | Leu | Pro | Phe | Leu |
| 15 | | | 35 | | | | | 40 | | | | | 45 | | | |
| | Thr | Thr | Glu | Val | Asn | Asn | Leu | Gly | Trp | Leu | Ser | Tyr | Gly | Ala | Leu | Lys |
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| | | Asp | Gly | Ile | Leu | Ile | Val | Val | Asn | Thr | Va1 | Gly | Ala | Ala | Leu | Gln |
| | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| 20 | Thr | Leu | Tyr | Ile | Leu | Ala | Tyr | Leu | His | Tyr | Cys | Pro | Arg | Lys | Arg | Val |
| | | | | | 85 | | | | | 90 | | | | | 95 | |
| | Val | Leu | Leu | Gln | Thr | Ala | Thr | Leu | Leu | Gly | Val | Leu | Leu | Leu | Gly | Tyr |
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| 0.5 | Gly | Tyr | | Trp | Leu | Leu | Val | | Asn | Pro | Glu | Åla | | Leu | Gln | Gln |
| 25 | | | 115 | | | | | 120 | | | | | 125 | | | |
| | Leu | | Leu | Phe | Cys | Ser | | Phe | Thr | Ile | Ser | Met | Tyr | Leu | Ser | Pro |
| | | 130 | | | | _ | 135 | | | | | 140 | | | | |
| | | Ala | Asp | Leu | Ala | | Val | Ile | Gln | Thr | | Ser | Thr | Gln | Cys | |
| 20 | 145 | m | | _ | | 150 | | | _ | | 155 | | | | | 160 |
| 30 | Ser | Tyr | Pro | Leu | | Ile | Ala | Thr | Leu | | Thr | Ser | Ala | Ser | | Cys |
| | • | m | | | 165 | _ | | | _ | 170 | | | | | 175 | |
| | Leu | туг | Gly | Phe | Arg | Leu | Arg | Asp | | Tyr | Ile | Met | Val | | Asn | Phe |
| | _ | | | 180 | | _ | | | 185 | | | | | 190 | | |
| 25 | Pro | GIÀ | | Val | Thr | Ser | Phe | | Arg | Phe | Trp | Leu | | Trp | Lys | Tyr |
| 35 | D | 0.1 | 195 | | | | | 200 | | | | | 205 | | | |
| | rro | | Glu | Gln | Asp | Arg | | Tyr | Trp | Leu | Leu | | Thr | | | |
| | | 210 | | | | | 215 | | | | | 220 | | | | |

| | | | | | | | | | | 90 | • | | | | | |
|------|-----|-----|------|------|------|------|-------------|------|------|------|-----|-----|-----|-----|-----|-----|
| | (2) | INF | ORMA | TION | FOR | SEQ | ID | NO: | 6: | • | | | | | | |
| | | | | EQUE | | | | | | | | | | | | |
| | | | | (A) | LEN | GTH: | 251 | | | | | | | | | |
| | | | | (B) | TYP | E: A | mino | aci | d | | | • | | | | |
| 5 | | | | (D) | TOP | OLOG | Y: L | inea | r | | | | | | | |
| | | (| ii) | SEQU | ENCE | KIN | D: P | rote | in | | | | | | | |
| | | (| iii) | HYP | OTHE | TICA | L: N | 0 | | | | | | | | |
| | | , | | | | | | | | | | | | | | |
| | | (| vi) | ORIG | INAL | sou | RCE: | | | | | | | | | |
| . 10 | | | | (A) | ORG | ANIS | M: <i>H</i> | omo | sapi | ens | | | | | | |
| | | | | (B) | CEL | L KI | ND: | Stom | ach | canc | er | | | | | |
| • | | | | (D) | CLO | NE N | AME: | HP1 | 0230 | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | | (: | xi) | SEQU | ENCE | DES | CRIP | TION | : SE | Q ID | NO: | 6: | | | | |
| 15 | | | | | | | | | | | | | | | | |
| | Met | Ser | Asp | Ile | Gly | Asp | Trp | Phe | Arg | Ser | Ile | Pro | Ala | Ile | Thr | Arg |
| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| | Tyr | Trp | Phe | Ala | Ala | Thr | Val | Ala | Val | Pro | Leu | Val | Gly | Lys | Leu | Gly |
| | | | | 20 | | | | | 25 | | | | | 30 | | |
| 20 | Leu | Ile | Ser | Pro | Ala | Tyr | Leu | Phe | Leu | Trp | Pro | Glu | Ala | Phe | Leu | Tyr |
| | | | 35 | | | | | 40 | | | | | 45 | | | |
| | Arg | Phe | Gln | Ile | Trp | Arg | Pro | Ile | Thr | Ala | Thr | Phe | Tyr | Phe | Pro | Val |
| | | 50 | | | | | 55 | • | | | | 60 | | | | |
| | | Pro | Gly | Thr | Gly | Phe | Leu | Tyr | Leu | Val | Asn | Leu | Tyr | Phe | Leu | Tyr |
| 25 | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| | Gln | Tyr | Ser | Thr | _ | Leu | Glu | Thr | Gly | Ala | Phe | Asp | Gly | Arg | Pro | Ala |
| | | | | | 85 | | | | | 90 | | | | | 95 | |
| | Asp | Tyr | Leu | Phe | Met | Leu | Leu | Phe | Asn | Trp | Ile | Cys | Ile | Val | Ile | Thr |
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| 30 | Gly | Leu | Ala | Met | Asp | Met | Gln | Leu | Leu | Met | Ile | Pro | Leu | Ile | Met | Ser |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| | Val | | Tyr | Val | Trp | Ala | | Leu | Asn | Arg | Asp | Met | Ile | Val | Ser | Phe |
| | | 130 | | | | | 135 | | | | | 140 | | | | |

Trp Phe Gly Thr Arg Phe Lys Ala Cys Tyr Leu Pro Trp Val Ile Leu

Gly Phe Asn Tyr Ile Ile Gly Gly Ser Val Ile Asn Glu Leu Ile Gly

Asn Leu Val Gly His Leu Tyr Phe Phe Leu Met Phe Arg Tyr Pro Met

155

170

150

165

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| | | | 180 | | | | | 185 | | | | | 190 | | |
|----|--------|-------|--------|-----------|-------|--------|--------|------|-------|------------|------|-----|-----|-----|-----|
| | Asp L | eu Gl | y Gly | Arg | Asn | Phe | Leu | Ser | Thr | Pro | Gln | Phe | Leu | Tyr | Ar |
| | | 19 | 5 | | | | 200 | | | | | 205 | | | |
| | Trp L | eu Pr | o Ser | Arg | Arg | Gly | Gly | Va1 | Ser | Gly | Phe | Gly | Val | Pro | Pr |
| 5 | 2 | 10 | | | | 215 | | | | | 220 | | | | |
| | Ala S | er Me | t Arg | Arg | Ala | Ala | Asp | Gln | Asn | Gly | Gly | Gly | Gly | Arg | Hi |
| | 225 | | | | 230 | | | | | 235 | | | | | 24 |
| | Asn T | rp Gl | y Gln | Gly | Phe | Arg | Leu | Gly | Asp | Gln | | | | | |
| | | | | 245 | | | | | 250 | | | | | • | |
| 10 | | | | | ٠ | | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| | (2) I | NFORM | ATION | FOR | SEQ | ID I | 10: | 7: | | | | | | | |
| | • | (i) | SEQUE | | | | RIST | cs: | | | | | | | |
| | | | | LENG | | | | | | | • | | | | |
| 15 | | | | TYPI | | | | | | | | | | | |
| | | | • • | TOPO | | | | | | | | | | | |
| | | | SEQU | | | | | in | | | | | | | |
| | | (iii |) HYP | OTHE | CICAI | L: No |) | | | | | | | | |
| 20 | | | ODIO | T 2.7 A Y | 00111 | 202 | | | | | | | | | |
| 20 | | (V1) | ORIG | | | | | | | | | • | | | |
| | | | | ORGA | | | | - | | . . | | | | | |
| | | | | CELI | | | _ | rmoı | La CE | rcı | 10ma | | | | |
| | | | | | | | | 200 | | | | | | | |
| 25 | • | | (D) | CLON | KE IN | MAR: | пгіс | 1309 | | | | | | | |
| 23 | | (vi) | SEQU | FNCF | חקכנ | וטדסי | י אררי | S EC | חד ו | NO. | 7. | | | | |
| | | (**) | o DQ o | LINOE | |)KII I | 1011 | 310 | | NO: | 7; | | | | |
| | Met A | la Th | r Pro | G1v | Pro | Va1 | Ile | Pro | Glu | Val | Pro | Phe | G1u | Pro | Ser |
| | 1. | | | 5 | | | | | 10 | | | | | 15 | |
| 30 | Lys P | ro Pr | o Val | Ile | Glu | Gly | Leu | Ser | | Thr | Val | Tvr | Arg | | Pro |
| | • | | 20 | | | | | 25 | | | | -,- | 30 | | |
| | Glu Se | er Ph | | Glu | Lys | Phe | Val | | Lvs | Thr | Arg | Glu | | Pro | Val |
| | | 3 | | | • | | 40 | | , - | | 0 | 45 | | | |
| | Val Pr | | | Cys | Leu | Ala | | Ala | Ala | Ala | Leu | | Tyr | Gly | Leu |
| 35 | | 50 | | • | | 55 | _ | | _ | | 60 | | , - | , | |
| | Tyr Se | | e His | Arg | Gly | | Ser | Gln | Arg | Ser | | Leu | Met | Met | Arg |
| | 65 | | | _ | 70 | | | | 5 | 75 | | | | | ۵۸ |

Thr Arg Ile Ala Ala Gln Gly Phe Thr Val Ala Ala Ile Leu Leu Gly

WO 98/55508

92

85

90

95

Leu Ala Val Thr Ala Met Lys Ser Arg Pro 100 105

5

- (2) INFORMATION FOR SEQ ID NO: 8:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 78
- . 10
- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: Protein
- (iii) HYPOTHETICAL: No
- 15 (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10408
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr Leu Leu Gly Ser

.

20

10

15

Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu Lys Leu Lys Glu

25

30

Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe Leu Glu Leu Leu

35

40

45

Glu Lys Leu Cys Leu Leu His Leu Pro Ser Gly Thr Ser Val Thr
50 55 60

30 Leu His His Ala Arg Ser Gln His His Val Val Cys Asn Thr

70

65

- (2) INFORMATION FOR SEQ ID NO: 9:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 314
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear

PCT/JP98/02445 WO 98/55508

93

| (ii) SEQUENCE | KIND: | Protein |
|---------------|-------|---------|
|---------------|-------|---------|

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

5

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP10412

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

10 Met Val Ala Pro Val Trp Tyr Leu Val Ala Ala Ala Leu Leu Val Gly Phe Ile Leu Phe Leu Thr Arg Ser Arg Gly Arg Ala Ala Ser Ala Gly 25 15 Gln Glu Pro Leu His Asn Glu Glu Leu Ala Gly Ala Gly Arg Val Ala 35 40 45 Gln Pro Gly Pro Leu Glu Pro Glu Glu Pro Arg Ala Gly Gly Arg Pro Arg Arg Arg Arg Asp Leu Gly Ser Arg Leu Gln Ala Gln Arg Arg Ala 20 70 75 Gln Arg Val Ala Trp Ala Glu Ala Asp Glu Asn Glu Glu Glu Ala Val 90 Ile Leu Ala Gln Glu Glu Glu Gly Val Glu Lys Pro Ala Glu Thr His 105 25 Leu Ser Gly Lys Ile Gly Ala Lys Lys Leu Arg Lys Leu Glu Glu Lys 115 120 125 Gln Ala Arg Lys Ala Gln Arg Glu Ala Glu Glu Ala Glu Arg Glu Glu 135 Arg Lys Arg Leu Glu Ser Gln Arg Glu Ala Glu Trp Lys Lys Glu Glu 30 145 150 Glu Arg Leu Arg Leu Glu Glu Glu Glu Glu Glu Glu Glu Arg Lys 170 Ala Arg Glu Glu Gln Ala Gln Arg Glu His Glu Glu Tyr Leu Lys Leu 180 185 Lys Glu Ala Phe Val Val Glu Glu Glu Gly Val Gly Glu Thr Met Thr 195 200 Glu Glu Gln Ser Gln Ser Phe Leu Thr Glu Phe Ile Asn Tyr Ile Lys 220 215

94

| | Gln | Ser | Lys | Val | Val | Leu | Leu | Glu | Asp | Leu | Ala | Ser | Gln | Val | Gly | Le |
|----|-----|-----|-------|------|-------|-------|-------|-------|-------|------|-----|-----|-----|-----|-----|-----|
| | 225 | | | | | 230 | | | | | 235 | | | | | 24 |
| | Arg | Thr | Gln | Asp | Thr | Ile | Asn | Arg | Ile | Gln | Asp | Leu | Leu | Ala | Glu | G1; |
| | | | | | 245 | | | | | 250 | | | | | 255 | |
| 5 | Thr | Ile | Thr | Gly | Val | Ile | Asp | Asp | Arg | Gly | Lys | Phe | Ile | Tyr | Ile | Th |
| | | | • | 260 | | | | | 265 | | | | | 270 | | |
| | Pro | G1u | Glu | Leu | Ala | Ala | Val | Ala | Asn | Phe | Ile | Arg | Gln | Arg | Gly | Arg |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| | Val | Ser | Ile | Ala | Glu | Leu | Ala | Gln | Ala | Ser | Asn | Ser | Leu | Ile | Ala | Tr |
| 10 | | 290 | | | | | 295 | | | | | 300 | | | | |
| | Gly | Arg | G1u | Ser | Pro | Ala | Gln | Ala | Pro | Ala | | | | | | |
| | 305 | | | | | 310 | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| 15 | (2) | INF | ORMA' | rion | FOR | SEQ | ID N | 10: 1 | LO: | | | | | | | |
| | | (i | i) SI | EQUE | ICE (| CHAR! | CTE | RIST | cs: | | | | | | | |
| | | | | (A) | LENG | TH: | 195 | | | | | | | | | |
| | | | | (B) | TYPI | E: An | nino | acid | i | | | | | | | |
| | | | | (D) | TOPO | LOGY | : Li | inear | : | | | | | | | |
| 20 | | (i | li) S | EQUE | ENCE | KINI | e Pr | rotei | in | | | | | | | |
| | | (i | Lii) | HYPO | THE | CICAI | .: No |) | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | | (3 | /i) (| RIG | NAL | SOUT | RCE: | | | | | | | | | |
| | | | | (A) | ORGA | NISN | 1: H | ото в | sapie | ens | | | | | | |
| 25 | | | | (B) | CELI | L KIN | TD: 5 | Stome | ch c | ance | er | | | | | |
| | | | | (D) | CLO | NE NA | ME: | HP10 | 1413 | | | | | | | |
| | | | | | | | | | | | | | | * | | |
| | | () | ci) S | EQUE | ENCE | DESC | RIPI | ION: | SEC |] ID | NO: | 10: | | | | |
| | | | | | | | | | | | | | | | | |
| 30 | Met | Ala | Ala | Glu | Asp | Val | Val | Ala | Thr | Gly | Ala | Asp | Pro | Ser | Asp | Leu |
| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| | Glu | Ser | Gly | G1y | Leu | Leu | His | Glu | Ile | Phe | Thr | Ser | Pro | Leu | Asn | Leu |
| | | | | 20 | | | | | 25 | | | | | 30 | | |
| | Leu | Leu | Leu | Gly | Leu | Cys | Ile | Phe | Leu | Leu | Tyr | Lys | Ile | Val | Arg | Gly |
| 35 | | | 35 | - | | | | 40 | | | - | - | 45 | | | |
| | Asp | Gln | Pro | Ala | Ala | Ser | Gly | Asp | Ser | Asp | Asp | Asp | Glu | Pro | Pro | Pro |
| | • | 50 | | | | | 55 | • | | • | • | 60 | | | | |

Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro Ala Glu Leu Arg Arg

95

65 7Ò 75 80 Phe Asp Gly Val Gln Asp Pro Arg Ile Leu Met Ala Ile Asn Gly Lys 85 90 Val Phe Asp Val Thr Lys Gly Arg Lys Phe Tyr Gly Pro Glu Gly Pro 5 105 Tyr Gly Val Phe Ala Gly Arg Asp Ala Ser Arg Gly Leu Ala Thr Phe 115 Cys Leu Asp Lys Glu Ala Leu Lys Asp Glu Tyr Asp Asp Leu Ser Asp 135 140 10 Leu Thr Ala Ala Gln Gln Glu Thr Leu Ser Asp Trp Glu Ser Gln Phe 145 150 160 155 Thr Phe Lys Tyr His His Val Gly Lys Leu Leu Lys Glu Gly Glu Glu 165 170 Pro Thr Val Tyr Ser Asp Glu Glu Glu Pro Lys Asp Glu Ser Ala Arg 15 185 190 Lys Asn Asp 195 20 (2) INFORMATION FOR SEQ ID NO: 11: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 462

- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- 25 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10415

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

35 Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu Ala Leu Val Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala Ala Gly Ile 20 30 25

| | Pro | Gly | Ile | Thr | Pro | Thr | Glu | Glu | Lys | Asp | Gly | Asn | Leu | Pro | Asp | Ile |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | 35 | | | | | 40 | | | | | 45 | | | |
| | Val | Asn | Ser | Gly | Ser | Leu | His | Glu | Phe | Leu | Val | Asn | Leu | His | Glu | Arg |
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| 5 | Tyr | Gly | Pro | Val | Val | Ser | Phe | Trp | Phe | Gly | Arg | Arg | Leu | Val | Val | Ser |
| | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| | Leu | Gly | Thr | Val | Asp | Val | Leu | Lys | Gln | His | Ile | Asn | Pro | Asn | Lys | Thr |
| | | | | | 85 | | | | | 90 | | | | | 95 | |
| | Leu | Asp | Pro | Phe | Glu | Thr | Met | Leu | Lys | Ser | Leu | Leu | Arg | Tyr | Gln | Ser |
| 10 | | | | 100 | | | | | 105 | | | | | 110 | | |
| | Gly | Gly | Gly | Ser | Val | Ser | Glu | Asn | His | Met | Arg | Lys | Lys | Leu | Tyr | Glu |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| | Asn | Gly | Val | Thr | Asp | Ser | Leu | Lys | Ser | Asn | Phe | Ala | Leu | Leu | Leu | Lys |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| 15 | Leu | Ser | Glu | Glu | Leu | Leu | Asp | Lys | Trp | Leu | Ser | Tyr | Pro | Glu | Thr | Gln |
| | 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| | His | Val | Pro | Leu | Ser | Gln | His | Met | Leu | Gly | Phe | Ala | Met | Lys | Ser | Val |
| | | | | | 165 | | | | | 170 | | | | | 175 | |
| | Thr | Gln | Met | Val | Met | Gly | Ser | Thr | Phe | Glu | Asp | Asp | Gln | Glu | Val | Ile |
| 20 | | | | 180 | | | | | 185 | | | | | 190 | | |
| | Arg | Phe | Gln | Lys | Asn | His | Gly | Thr | Val | Trp | Ser | Glu | Ile | Gly | Lys | Gly |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| | Phe | Leu | Asp | Gly | Ser | Leu | Asp | Lys | Asn | Met | Thr | Arg | Lys | Lys | Gln | Tyr |
| | | 210 | | | | | 215 | | | | | 220 | | | | |
| 25 | Glu | Asp | Ala | Leu | Met | Gln | Leu | Glu | Ser | Val | Leu | Arg | Asn | Ile | Ile | Lys |
| | 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| | Glu | Arg | Lys | Gly | Arg | Asn | Phe | Ser | Gln | His | Ile | Phe | Ile | Asp | Ser | Leu |
| | | | | | 245 | | | | | 250 | | | | | 255 | |
| | Val | Gln | Gly | Asn | Leu | Asn | Asp | Gln | Gln | Ile | Leu | Glu | Asp | Ser | Met | Ile |
| 30 | | | | 260 | | | | | 265 | | | | | 270 | | |
| | Phe | Ser | Leu | Ala | Ser | Cys | Ile | Ile | Thr | Ala | Lys | Leu | Cys | Thr | Trp | Ala |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| | Ile | Cys | Phe | Leu | Thr | Thr | Ser | Glu | Glu | Val | Gln | Lys | Lys | Leu | Tyr | Glu |
| | | 290 | | | | | 295 | | | | | 300 | | | | |
| 35 | Glu | Ile | Asn | Gln | Val | Phe | Gly | Asn | Gly | Pro | Val | Thr | Pro | Glu | Lys | Ile |
| | 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| | Glu | Gln | Leu | Arg | Tyr | Cys | Gln | His | Val | Leu | Cys | Glu | Thr | Val | Arg | Thr |
| | | | | | 325 | | | | | 330 | | | | | 335 | |

97

| | | | | | | | | | | - | | | | | | |
|----|-----|------|-------|-----|------|-----|------|-------|-----|-----|-----|-----|-----|-----|-----|-----|
| | Ala | Lys | Leu | Thr | Pro | Val | Ser | Ala | Gln | Leu | Gln | Asp | Ile | Glu | Gly | Lys |
| | | | | 340 | | | | | 345 | | | | | 350 | | |
| | Ile | Asp | Arg | Phe | Ile | Ile | Pro | Arg | Glu | Thr | Leu | Val | Leu | Tyr | Ala | Leu |
| | | | 355 | | | | | 360 | | | | | 365 | | | |
| 5 | Gly | Val | Val | Leu | Gln | Asp | Pro | Asn | Thr | Trp | Pro | Ser | Pro | His | Lys | Phe |
| | | 370 | | | | | 375 | | | | | 380 | | | | |
| | Asp | Pro | Asp | Arg | Phe | Asp | Asp | Glu | Leu | Val | Met | Lys | Thr | Phe | Ser | Ser |
| | 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| | Leu | Gly | Phe | Ser | Gly | Thr | Gln | Glu | Cys | Pro | G1u | Leu | Arg | Phe | Ala | Tyr |
| 10 | | | | | 405 | | | | | 410 | | | • | | 415 | |
| | Met | Val | Thr | Thr | Val | Leu | Leu | Ser | Val | Leu | Val | Lys | Arg | Leu | His | Leu |
| | | | | 420 | | | | | 425 | | | | | 430 | | |
| | Leu | Ser | Val | Glu | Gly | Gln | Val | Ile | Glu | Thr | Lys | Tyr | Glu | Leu | Val | Thr |
| | | | 435 | | | | | 440 | | | | | 445 | | | |
| 15 | Ser | Ser | Arg | Glu | Glu | Ala | Trp | Ile | Thr | Val | Ser | Lys | Arg | Tyr | | |
| | | 450 | | | | | 455 | | | | | 460 | | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | (2) | TNEC | NDMAT | KOT | EUD. | CEA | TD N | 10. 1 | 2. | | | | | | | |

INFORMATION FOR SEQ ID NO: 12:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 247
- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: Protein
- 25 (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- 30 (D) CLONE NAME: HP10419

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Met Gly Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro 35 10 Ala Phe Ala Leu Phe Leu Ile Thr Val Ala Gly Asp Pro Leu Arg Val 25 Ile Ile Leu Val Ala Gly Ala Phe Phe Trp Leu Val Ser Leu Leu Leu

| • | | | 35 | | | | | 40 | | | | | 45 | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | Ala | Ser | Val | Val | Trp | Phe | Ile | Leu | Val | His | Val | Thr | Asp | Arg | Ser | As |
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| | Ala | Arg | Leu | Gln | Tyr | Gly | Leu | Leu | Ile | Phe | Gly | Ala | Ala | Val | Ser | Va. |
| 5 | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| | Leu | Leu | Gln | Glu | Val | Phe | Arg | Phe | Ala | Tyr | Tyr | Lys | Leu | Leu | Lys | Ly |
| | | | | | 85 | | | | | 90 | | | | | 95 | |
| | Ala | Asp | Glu | Gly | Leu | Ala | Ser | Leu | Ser | Glu | Asp | Gly | Arg | Ser | Pro | Ile |
| | | | | 100 | • | | | | 105 | | | | • | 110 | | |
| 10 | Ser | Ile | Arg | Gln | Met | Ala | Tyr | Val | Ser | Gly | Leu | Ser | Phe | Gly | Ile | Ile |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| | Ser | G1y | Val | Phe | Ser | Val | Ile | Asn | Ile | Leu | Ala | Asp | Ala | Leu | Gly | Pro |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| | Gly | Val | Val | Gly | Ile | His | G1y | Asp | Ser | Pro | Tyr | Tyr | Phe | Leu | Thr | Ser |
| 15 | 145 | | | | | 150 | | | | | 155 | • | | | | 160 |
| | Ala | Phe | Leu | Thr | Ala | A1a | Ile | Ile | Leu | Leu | His | Thr | Phe | Trp | Gly | Val |
| | | | | | 165 | | | | | 170 | | | | | 175 | |
| | Val | Phe | Phe | Asp | Ala | Cys | Glu | Arg | Arg | Arg | Tyr | Trp | Ala | Leu | Gly | Leu |
| | | | | 180 | | | | | 185 | | | | | 190 | | |
| 20 | Val | Val | | Ser | His | Leu | Leu | Thr | Ser | Gly | Leu | Thr | Phe | Leu | Asn | Pro |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| | | | Glu | Ala | Ser | Leu | | Pro | Ile | Tyr | Ala | Val | Thr | Val | Ser | Met |
| | | 210 | | | | | 215 | | | | | 220 | | | | |
| | | Leu | Trp | Ala | Phe | | Thr | Ala | Gly | Gly | Ser | Leu | Arg | Ser | Ile | |
| 25 | 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| | Arg | Ser | Leu | Leu | - | Lys | Asp | | | | | | | • | | |
| | | | | | 245 | | | | | | | | | | | |

- 30 (2) INFORMATION FOR SEQ ID NO: 13:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 35 (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:

99

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10424

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Met Asn Phe Tyr Leu Leu Leu Ala Ser Ser Ile Leu Cys Ala Leu Ile

5 10 1

Val Phe Trp Lys Tyr Arg Arg Phe Gln Arg Asn Thr Gly Glu Met Ser

10 20 25 30

Ser Asn Ser Thr Ala Leu Ala Leu Val Arg Pro Ser Ser Ser Gly Leu

35 40 45

Ile Asn Ser Asn Thr Asp Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg

50 55 60

15 Asp Ile Leu Asn Asn Phe Pro His Ser Ile Ala Arg Gln Lys Arg Ile

65 70 75 80

Leu Val Asn Leu Ser Met Val Glu Asn Lys Leu Val Glu Leu Glu His
85 90 95

Thr Leu Leu Ser Lys Gly Phe Arg Gly Ala Ser Pro His Arg Lys Ser

20 100 105 110

Thr

- (2) INFORMATION FOR SEQ ID NO: 14:
- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 365
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
- 30 (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Epidermoid carcinoma
- 35 (C) CELL LINE: KB
 - (D) CLONE NAME: HP10428
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

| | Met | Gly | Arg | Trp | Ala | Leu | Asp | Val | Ala | Phe | Leu | Trp | Lys | Ala | Val | Let |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| | Thr | Leu | Gly | Leu | Val | Leu | Leu | Tyr | Tyr | Cys | Phe | Ser | Ile | Gly | Ile | Thr |
| | | | | 20 | | | | | 25 | | | | | 30 | | |
| 5 | Phe | Tyr | Asn | Lys | Trp | Leu | Thr | Lys | Ser | Phe | His | Phe | Pro | Leu | Phe | Met |
| | | | 35 | | | | | 40 | | | | | 45 | | | |
| | Thr | Met | Leu | His | Leu | Ala | Va1 | Ile | Phe | Leu | Phe | Ser | Ala | Leu | Ser | Arg |
| | | 50 | | | | | 55 | | | | | 60 | | • | | |
| | Ala | Leu | Val | Gln | Cys | Ser | Ser | His | Arg | Ala | Arg | Val | Val | Leu | Ser | Trp |
| 10 | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| | Ala | Asp | Tyr | Leu | Arg | Arg | Val | Ala | Pro | Thr | Ala | Leu | Ala | Thr | Ala | Leu |
| | | | • | | 85 | | | | | 90 | | | | | 95 | |
| | Asp | Val | Gly | Leu | Ser | Asn | Trp | Ser | Phe | Leu | Tyr | Va1 | Thr | Val | Ser | Leu |
| | | | | 100 | | | | | 105 | | | | | 110 | | |
| 15 | Tyr | Thr | Met | Thr | Lys | Ser | Ser | Ala | Va1 | Leu | Phe | Ile | Leu | Ile | Phe | Ser |
| | | | 115 | | | | | 120 | | | | | 125 | | | |
| | Leu | Ile | Phe | Lys | Leu | Glu | Glu | Leu | Arg | Ala | Ala | Leu | Val | Leu | Val | Val |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| | Leu | Leu | Ile | Ala | Gly | Gly | Leu | Phe | Met | Phe | Thr | Tyr | Lys | Ser | Thr | Gln |
| 20 | 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| | Phe | Asn | Val | Glu | Gly | Phe | Ala | Leu | Val | Leu | Gly | Ala | Ser | Phe | Ile | Gly |
| | | | | | 165 | | | | | 170 | | | | | 175 | |
| | Gly | Ile | Arg | Trp | Thr | Leu | Thr | Gln | Met | Leu | Leu | Gln | Lys | Ala | G1u | Leu |
| | | | | 180 | | | | | 185 | | | | | 190 | | |
| 25 | Gly | Leu | Gln | Asn | Pro | Ile | Asp | Thr | Met | Phe | His | Leu | Gln | Pro | Leu | Met |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| | Phe | Leu | Gly | Leu | Phe | Pro | Leu | Phe | Ala | Val | Phe | Glu | Gly | Leu | His | Leu |
| | | 210 | | | | | 215 | | | | | 220 | | | | |
| | Ser | Thr | Ser | Glu | Lys | Ile | Phe | Arg | Phe | Gln | Asp | Thr | Gly | Leu | Leu | Leu |
| 30 | 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| | Arg | Va1 | Leu | Gly | Ser | Leu | Phe | Leu | Gly | Gly | Ile | Leu | Ala | Phe | Gly | Leu |
| | | | | | 245 | | | | | 250 | | | | | 255 | |
| | G1y | Phe | Ser | Glu | Phe | Leu | Leu | Val | Ser | Arg | Thr | Ser | Ser | Leu | Thr | Leu |
| | | | | 260 | | | | | 265 | | | | | 270 | | |
| 35 | Ser | Ile | Ala | Gly | Ile | Phe | Lys | Glu | Val | Cys | Thr | Leu | Leu | Leu | Ala | Ala |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| | His | Leu | Leu | Gly | Asp | Gln | Ile | Ser | Leu | Leu | Asn | Trp | Leu | Gly | Phe | Ala |
| | | 290 | | | | | 295 | | | | | 300 | | | | |

101

Leu Cys Leu Ser Gly Ile Ser Leu His Val Ala Leu Lys Ala Leu His 305 310 315 Ser Arg Gly Asp Gly Gly Pro Lys Ala Leu Lys Gly Leu Gly Ser Ser 325 330 Pro Asp Leu Glu Leu Leu Arg Ser Ser Gln Arg Glu Glu Gly Asp 345 Asn Glu Glu Glu Tyr Phe Val Ala Gln Gly Gln Gln 355 360 365 10 (2) INFORMATION FOR SEQ ID NO: 15: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 226 (B) TYPE: Amino acid 15 (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No (vi) ORIGINAL SOURCE: 20 (A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10429 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15: 25 Met Pro Thr Thr Lys Lys Thr Leu Met Phe Leu Ser Ser Phe Phe Thr Ser Leu Gly Ser Phe Ile Val Ile Cys Ser Ile Leu Gly Thr Gln Ala 25 Trp Ile Thr Ser Thr Ile Ala Val Arg Asp Ser Ala Ser Asn Gly Ser 35 45 Ile Phe Ile Thr Tyr Gly Leu Phe Arg Gly Glu Ser Ser Glu Glu Leu 55 60 Ser His Gly Leu Ala Glu Pro Lys Lys Phe Ala Val Leu Glu Ile 35

70

Leu Asn Asn Ser Ser Gln Lys Thr Leu His Ser Val Thr Ile Leu Phe

Leu Val Leu Ser Leu Ile Thr Ser Leu Leu Ser Ser Gly Phe Thr Phe

75

90

102

100 105 110 Tyr Asn Ser Ile Ser Asn Pro Tyr Gln Thr Phe Leu Gly Pro Thr Gly 115 120 125 Val Tyr Thr Trp Asn Gly Leu Gly Ala Ser Phe Val Phe Val Thr Met 5 135 140 Ile Leu Phe Val Ala Asn Thr Gln Ser Asn Gln Leu Ser Glu Glu Leu 150 155 Phe Gln Met Leu Tyr Pro Ala Thr Thr Ser Lys Gly Thr Thr His Ser 165 170 10 Tyr Gly Tyr Ser Phe Trp Leu Ile Leu Leu Val Ile Leu Leu Asn Ile 180 185 Val Thr Val Thr Ile Ile Ile Phe Tyr Gln Lys Ala Arg Tyr Gln Arg 195 200 205 Lys Gln Glu Gln Arg Lys Pro Met Glu Tyr Ala Pro Arg Asp Gly Ile 15 215 220 Leu Phe 225

- 20 (2) INFORMATION FOR SEQ ID NO: 16:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 129
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 25 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP10432
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:
- 35 Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly

 1 5 10 15

 Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly

 20 25 30

WO 98/55508

103

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys 35 40 Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro 70 75 Ile Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser 85 90 Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Glu Lys Phe Thr Thr 10 105 Pro Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu Ile 115 120 125 Gln 15 (2) INFORMATION FOR SEQ ID NO: 17: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 163 20 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Liver (D) CLONE NAME: HP10433 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17: Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly Ala Val Gly Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Arg Gly Leu Gln Val 35 20 25 30 Ala Leu Glu Glu Phe His Lys His Pro Pro Val Gln Trp Ala Phe Gln 40

Glu Thr Ser Val Glu Ser Ala Val Asp Thr Pro Phe Pro Ala Gly Ile

104

50 60 55 Phe Val Arg Leu Glu Phe Lys Leu Gln Gln Thr Ser Cys Arg Lys Arg 65 70 75 Asp Trp Lys Lys Pro Glu Cys Lys Val Arg Pro Asn Gly Arg Lys Arg 90 Lys Cys Leu Ala Cys Ile Lys Leu Gly Ser Glu Asp Lys Val Leu Gly 100 105 110 Arg Leu Val His Cys Pro Ile Glu Thr Gln Val Leu Arg Glu Ala Glu 120 10 Glu His Gln Glu Thr Gln Cys Leu Arg Val Gln Arg Ala Gly Glu Asp 135 Pro His Ser Phe Tyr Phe Pro Gly Gln Phe Ala Phe Ser Lys Ala Leu 145 150 155 Pro Arg Ser 15 (2) INFORMATION FOR SEQ ID NO: 18: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 193 20 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10480 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18: Met Ile Arg Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro 1 5 10 Leu Leu Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly 35 20 Arg Gly Trp Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp 40

Trp Lys Cys Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly

| | | 50 | | | | | 55 | | | | | 60 | | | | | |
|-----|------|------|--------|-----------------|----------|----------------|-------|-----------------|-------|-----------|------|---------------|-------|-------|-------|-------|-----|
| | Cys | Gln | Ser | Leu | Met | Glu | Tyr | Ala | Trp | Gly | Arg | Ala | Ala | Ala | Ala | Met | |
| | 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| | Leu | Phe | Cys | Gly | Phe | Ile | Ile | Leu | Val | Ile | Cys | Phe | Ile | Leu | Ser | Phe | |
| 5 | | | | | 85 | | | | | 90 | | | | | 95 | | |
| | Phe | Ala | Leu | Cys | G1y | Pro | Gln | Met | Leu | Val | Phe | Leu | Arg | Val | Ile | Gly | |
| | | | | 100 | | | | | 105 | | | | | 110 | | | |
| | Gly | Leu | Leu | Ala | Leu | Ala | Ala | Val | Phe | Gln | Ile | Ile | Ser | Leu | Val | Ile | |
| | | | 115 | | | | | 120 | | | | | 125 | | | | |
| 10 | Tyr | Pro | Val | Lys | Tyr | Thr | Gln | Thr | Phe | Thr | Leu | His | Ala | Asn | Arg | Ala | |
| | | 130 | | | | | 135 | | | | | 140 | | | | | |
| | Val | Thr | Tyr | Ile | Tyr | Asn | Trp | Ala | Tyr | Gly | Phe | Gly | Trp | Ala | Ala | Thr | |
| | 145 | | • | | | 150 | | | | | 155 | | | | | 160 | |
| | Ile | Ile | Leu | Ile | Gly | Сув | Ala | Phe | Phe | Phe | Cys | Cys | Leu | Pro | Asn | Tyr | |
| 15 | | | | | 165 | | | | | 170 | | | | | 175 | | |
| | Glu | Asp | Asp | Leu | Leu | Gly | Asn | Ala | Lys | Pro | Arg | Tyr | Phe | Tyr | Thr | Ser | |
| | | | | 180 | | | | | 185 | | | | | 190 | | | |
| | Ala | | | | | | | | | | | | | | | | |
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| | (2) | | | | | SEQ | | | | | | | | | | | |
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| | | | | | | GTH: | | | | | | | | | | • | • |
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| | | | | (1) | CLUI | 1€ NA | nic: | ULOI | .203 | | | | | | | | |
| | | (* | ri) c | יוו רש: | מרבי | DESC | יפדקי | - זאר) די | . CEC | חדו | NO - | 10. | | | | | |
| 35 | | () | .1) 2 | יבעטו | LIVE | שנטע | MIFI | TON |) DEC | (דח | MO: | TA: | | | | | |
| , , | ATGO | CTCT | ים מפי | ነርርጥባ | ימממי | ነጥ ርር | CACT | ነር ጥ ር ር | ነ ልጥሮ | ነርጥልብ | ጥርር | ም ር ሞር | :CTGC | :CC 4 | GCA A | TGTCT | ' 6 |
| | | | | | | | | | | | | | | | | CCGAT | |
| | | | | | | 171 CC | | | | , o 1 o 1 | 404 | 4466 | 0100 | | 01101 | COMAM | 10 |

| | GTGCTGAGAC | TCAACCGAGT | GAACGACGCC | CAGGAATACA | GACGGGGTGG | CCTGGGATCT | 240 |
|----|------------|------------|------------|------------|------------|------------|------|
| | CTGTTCTATC | TTACACTGGA | TGTGCTAGAG | ACTGACTGCC | ATGTGCTCAG | AAAGAAGGCA | 300 |
| | TGGCAAGACT | GTGGAATGAG | GATATTTTT | GAATCAGTTT | ATGGTCAATG | CAAAGCAATA | 360 |
| | TTTTATATGA | ACAACCCAAG | TAGAGTTCTC | TATTTAGCTG | CTTATAACTG | TACTCTTCGC | 420 |
| 5 | CCAGTTTCAA | AAAAAAAGAT | TTACATGACG | TGCCCTGACT | GCCCAAGCTC | CATACCCACT | 480 |
| | GACTCTTCCA | ATCACCAAGT | GCTGGAGGCT | GCCACCGAGT | CTCTTGCGAA | ATACAACAAT | 540 |
| | GAGAACACAT | CCAAGCAGTA | TTCTCTCTTC | AAAGTCACCA | GGGCTTCTAG | CCAGTGGGTG | 600 |
| | GTCGGCCCTT | CTTACTTTGT | GGAATACTTA | ATTAAAGAAT | CACCATGTAC | TAAATCCCAG | 660 |
| | GCCAGCAGCT | GTTCACTTCA | GTCCTCCGAC | TCTGTGCCTG | TTGGTCTTTG | CAAAGGTTCT | 720 |
| 10 | CTGACTCGAA | CACACTGGGA | AAAGTTTGTC | TCTGTGACTT | GTGACTTCTT | TGAATCACAG | 780 |
| | GCTCCAGCCA | CTGGAAGTGA | AAACTCTGCT | GTTAACCAGA | AACCTACAAA | CCTTCCCAAG | 840 |
| | GTGGAAGAAT | CCCAGCAGAA | AAACACCCCC | CCAACAGACT | CCCCTCCAA | AGCTGGGCCA | 900 |
| | AGAGGATCTG | TCCAATATCT | TCCTGACTTG | GATGATAAAA | ATTCCCAGGA | AAAGGGCCCT | 960 |
| | CAGGAGGCCT | TTCCTGTGCA | TCTGGACCTA | ACCACGAATC | CCCAGGGAGA | AACCCTGGAT | 1020 |
| 15 | ATTTCCTTCC | TCTTCCTGGA | GCCTATGGAG | GAGAAGCTGG | TTGTCCTGCC | TTTCCCCAAA | 1080 |
| | GAAAAAGCAC | GCACTGCTGA | GTGCCCAGGG | CCAGCCCAGA | ATGCCAGCCC | TCTTGTCCTT | 1140 |
| | CCGCCA | | | | | | 1146 |
| | | | | | | | |

20 (2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 951
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 25 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP01299

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

| 3 | 35 | ATGTGGCTCT | ACCTGGCGGC | CTTCGTGGGC | CTGTACTACC | TTCTGCACTG | GTACCGGGAG | 60 |
|---|----|------------|------------|------------|------------|------------|------------|-----|
| | | AGGCAGGTGG | TGAGCCACCT | CCAAGACAAG | TATGTCTTTA | TCACGGGCTG | TGACTCGGGC | 120 |
| | | TTTGGGAACC | TGCTGGCCAG | ACAGCTGGAT | GCACGAGGCT | TGAGAGTGCT | GGCTGCGTGT | 180 |
| | | CTGACGGAGA | AGGGGGCCGA | GCAGCTGAGG | GGCCAGACGT | CTGACAGGCT | GGAGACGGTG | 240 |

| | ACCCTGGATG | TTACCAAGAT | GGAGAGCATC | GCŢGCAGCTA | CTCAGTGGGT | GAAGGAGCAT | 300 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | GTGGGGGACA | GAGGACTCTG | GGGACTGGTG | AACAATGCAG | GCATTCTTAC | ACCAATTACC | 360 |
| | TTATGTGAGT | GGCTGAACAC | TGAGGACTCT | ATGAATATGC | TCAAAGTGAA | CCTCATTGGT | 420 |
| | GTGATCCAGG | TGACCTTGAG | CATGCTTCCT | TTGGTGAGGA | GAGCACGGGG | AAGAATTGTC | 480 |
| 5 | AATGTCTCCA | GCATTCTGGG | AAGAGTTGCT | TTCTTTGTAG | GAGGCTACTG | TGTCTCCAAG | 540 |
| | TATGGAGTGG | AAGCCTTTTC | AGATATTCTG | AGGCGTGAGA | TTCAACATTT | TGGGGTGAAA | 600 |
| | ATCAGCATAG | TTGAACCTGG | CTACTTCAGA | ACGGGAATGA | CAAACATGAC | ACAGTCCTTA | 660 |
| | GAGCGAATGA | AGCAAAGTTG | GAAAGAAGCC | CCCAAGCATA | TTAAGGAGAC | CTATGGACAG | 720 |
| | CAGTATTTTG | ATGCCCTTTA | CAATATCATG | AAGGAAGGGC | TGTTGAATTG | TAGCACAAAC | 780 |
| 10 | CTGAACCTGG | TCACTGACTG | CATGGAACAT | GCTCTGACAT | CGGTGCATCC | GCGAACTCGA | 840 |
| | TATTCAGCTG | GCTGGGATGC | TAAATTTTTC | TTCATCCCTC | TATCTTATTT | ACCTACATCA | 900 |
| | CTGGCAGACT | ACATTTTGAC | TAGATCTTGG | CCCAAACCAG | CCCAGGCAGT | С | 951 |
| | | | | | | | |

15 (2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 888
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 20 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP01347

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

| 30 | ATGAGTGACT | CCAAGGAACC | AAGGGTGCAG | CAGCTGGGCC | TCCTGGGGTG | TCTTGGCCAT | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | GGCGCCCTGG | TGCTGCAACT | CCTCTCCTTC | ATGCTCTTGG | CTGGGGTCCT | GGTGGCCATC | 120 |
| | CTTGTCCAAG | TGTCCAAGGT | CCCCAGCTCC | CTAAGTCAGG | AACAATCCGA | GCAAGACGCA | 180 |
| | ATCTACCAGA | ACCTGACCCA | GCTTAAAGCT | GCAGTGGGTG | AGCTCTCAGA | GAAATCCAAG | 240 |
| | CTGCAGGAGA | TCTACCAGGA | GCTGACCCAG | CTGAAGGCTG | CAGTGGGTGA | GTTGCCAGAG | 300 |
| 35 | AAATCCAAGC | TGCAGGAGAT | CTACCAGGAG | CTGACCCGGC | TGAAGGCTGC | AGTGGGTGAG | 360 |
| | TTGCCAGAGA | AATCCAAGCT | GCAGGAGATC | TACCAGGAGC | TGACCCGGCT | GAAGGCTGCA | 420 |
| | GTGGGTGAGT | TGCCAGAGAA | ATCCAAGCTG | CAGGAGATCT | ACCAGGAGCT | GACCCGGCTG | 480 |
| | AAGGCTGCAG | TGGGTGAGTT | GCCAGAGAAA | TCCAAGCTGC | AGGAGATCTA | CCAGGAGCTG | 540 |

108

| | ACGGAGCTGA | AGGCTGCAGT | GGGTGAGTTG | CCAGAGAAAT | CCAAGCTGCA | GGAGATCTAC | 600 |
|---|------------|------------|------------|------------|------------|------------|-----|
| | CAGGAGCTGA | CCCAGCTGAA | GGCTGCAGTG | GGTGAGTTGC | CAGACCAGTC | CAAGCAGCAG | 660 |
| | CAAATCTATC | AAGAACTGAC | CGATTTGAAG | ACTGCATTTG | AACGCCTGTG | CCGCCACTGT | 720 |
| | CCCAAGGACT | GGACATTCTT | CCAAGGAAAC | TGTTACTTCA | TGTCTAACTC | CCAGCGGAAC | 780 |
| 5 | TGGCACGACT | CCGTCACCGC | CTGCCAGGAA | GTGAGGGCCC | AGCTCGTCGT | AATCAAAACT | 840 |
| | GCTGAGGAGC | AGCTTCCAGC | GGTACTGGAA | CAGTGGAGAA | CCCAACAA | | 888 |

(2) INFORMATION FOR SEQ ID NO: 22:

10 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 591
- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- 15 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- 20 (D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

| | ATGTGTACGG | GAAAATGTGC | CCGCTGTGTG | GGGCTCTCCC | TCATTACCCT | CTGCCTCGTC | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 25 | TGCATTGTGG | CCAACGCCCT | CCTGCTGGTA | CCTAATGGGG | AGACCTCCTG | GACCAACACC | 120 |
| | AACCATCTCA | GCTTGCAAGT | CTGGCTCATG | GGCGGCTTCA | TTGGCGGGGG | CCTAATGGTA | 180 |
| | CTGTGTCCGG | GGATTGCAGC | CGTTCGGGCA | GGGGGCAAGG | GCTGCTGTGG | TGCTGGGTGC | 240 |
| | TGTGGAAACC | GCTGCAGGAT | GCTGCGCTCG | GTCTTCTCCT | CGGCGTTCGG | GGTGCTTGGT | 300 |
| | GCCATCTACT | GCCTCTCGGT | GTCTGGAGCT | GGGCTCCGAA | ATGGACCCAG | ATGCTTAATG | 360 |
| 30 | AACGGCGAGT | GGGGCTACCA | CTTCGAAGAC | ACCGCGGGAG | CTTACTTGCT | CAACCGCACT | 420 |
| | CTATGGGATC | GGTGCGAGGC | GCCCCTCGC | GTGGTCCCCT | GGAATGTGAC | GCTCTTCTCG | 480 |
| | CTGCTGGTGG | CCGCCTCCTG | CCTGGAGATA | GTACTGTGTG | GGATCCAGCT | GGTGAACGCG | 540 |
| | ACCATTGGTG | TCTTCTGCGG | CGATTGCAGG | AAAAAACAGG | ACACCCCTCA | С | 591 |

- (2) INFORMATION FOR SEQ ID NO: 23:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 663

109

| (B) | TYPE: Nucleic | acid |
|-----|----------------|--------|
| (C) | STRANDEDNESS: | Double |
| (D) | TOPOLOGY: Line | ear |

(ii) SEQUENCE KIND: cDNA to mRNA

5

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP01526

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

ATGGAGGCGG GCGGCTTTCT GGACTCGCTC ATTTACGGAG CATGCGTGGT CTTCACCCTT 60 GGCATGTTCT CCGCCGGCCT CTCGGACCTC AGGCACATGC GAATGACCCG GAGTGTGGAC 120 15 AACGTCCAGT TCCTGCCCTT TCTCACCACG GAAGTCAACA ACCTGGGCTG GCTGAGTTAT 180 GGGGCTTTGA AGGGAGACGG GATCCTCATC GTCGTCAACA CAGTGGGTGC TGCGCTTCAG 240 ACCCTGTATA TCTTGGCATA TCTGCATTAC TGCCCTCGGA AGCGTGTTGT GCTCCTACAG 300 ACTGCAACCC TGCTAGGGGT CCTTCTCCTG GGTTATGGCT ACTTTTGGCT CCTGGTACCC 360 AACCCTGAGG CCCGGCTTCA GCAGTTGGGC CTCTTCTGCA GTGTCTTCAC CATCAGCATG 420 20 TACCTCTCAC CACTGGCTGA CTTGGCTAAG GTGATTCAAA CTAAATCAAC CCAATGTCTC 480 TCCTACCCAC TCACCATTGC TACCCTTCTC ACCTCTGCCT CCTGGTGCCT CTATGGGTTT 540 CGACTCAGAG ATCCCTATAT CATGGTGTCC AACTTTCCAG GAATCGTCAC CAGCTTTATC 600 CGCTTCTGGC TTTTCTGGAA GTACCCCCAG GAGCAAGACA GGAACTACTG GCTCCTGCAA 660 ACC 663

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(2) INFORMATION FOR SEQ ID NO: 24:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 753

30

- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: cDNA to mRNA

35 (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP10230

110

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

| | ATGTCGGACA | TCGGAGACTG | GTTCAGGAGC | ATCCCGGCGA | TCACGCGCTA | TTGGTTCGCC | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | GCCACCGTCG | CCGTGCCCTT | GGTCGGCAAA | CTCGGCCTCA | TCAGCCCGGC | CTACCTCTTC | 120 |
| 5 | CTCTGGCCCG | AAGCCTTCCT | TTATCGCTTT | CAGATTTGGA | GGCCAATCAC | TGCCACCTTT | 180 |
| | TATTTCCCTG | TGGGTCCAGG | AACTGGATTT | CTTTATTTGG | TCAATTTATA | TTTCTTATAT | 240 |
| | CAGTATTCTA | CGCGACTTGA | AACAGGAGCT | TTTGATGGGA | GGCCAGCAGA | CTATTTATTC | 300 |
| | ATGCTCCTCT | TTAACTGGAT | TTGCATCGTG | ATTACTGGCT | TAGCAATGGA | TATGCAGTTG | 360 |
| | CTGATGATTC | CTCTGATCAT | GTCAGTACTT | TATGTCTGGG | CCCAGCTGAA | CAGAGACATG | 420 |
| 10 | ATTGTATCAT | TTTGGTTTGG | AACACGATTT | AAGGCCTGCT | ATTTACCCTG | GGTTATCCTT | 480 |
| | GGATTCAACT | ATATCATCGG | AGGCTCGGTA | ATCAATGAGC | TTATTGGAAA | TCTGGTTGGA | 540 |
| | CATCTTTATT | TTTTCCTAAT | GTTCAGATAC | CCAATGGACT | TGGGAGGAAG | AAATTTTCTA | 600 |
| | TCCACACCTC | AGTTTTTGTA | CCGCTGGCTG | CCCAGTAGGA | GAGGAGGAGT | ATCAGGATTT | 660 |
| | GGTGTGCCCC | CTGCTAGCAT | GAGGCGAGCT | GCTGATCAGA | ATGGCGGAGG | CGGGAGACAC | 720 |
| 15 | AACTGGGGCC | AGGGCTTTCG | ACTTGGAGAC | CAG | | | 753 |
| | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

20

- (A) LENGTH: 318
- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: cDNA to mRNA

25

- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Epidermoid carcinoma
 - (C) CELL LINE: KB

30

(D) CLONE NAME: HP10389

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

| | ATGGCGACTC | CCGGCCCTGT | GATTCCGGAG | GTCCCCTTTG | AACCATCGAA | GCCTCCAGTC | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 35 | ATTGAGGGGC | TGAGCCCCAC | TGTTTACAGG | AATCCAGAGA | GTTTCAAGGA | AAAGTTCGTT | 120 |
| | CGCAAGACCC | GCGAGAACCC | GGTGGTACCC | ATAGGTTGCC | TGGCCACGGC | GGCCGCCCTC | 180 |
| | ACCTACGGCC | TCTACTCCTT | CCACCGGGGC | AACAGCCAGC | GCTCTCAGCT | CATGATGCGC | 240 |
| | ACCCGGATCG | CCGCCCAGGG | TTTCACGGTC | GCAGCCATCT | TGCTGGGTCT | GGCTGTCACT | 300 |

111

318

GCTATGAAGT CTCGACCC

| | (2) INFORMATION FOR SEQ ID NO: 26: | |
|----|---|-----|
| 5 | (1) SEQUENCE CHARACTERISTICS: | |
| J | (A) LENGTH: 234 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| | (D) TOPOLOGY: Linear | |
| 10 | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| | (B) CELL KIND: Stomach cancer | |
| 15 | (D) CLONE NAME: HP10408 | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26: | |
| | ATGGGGTCTG GGCTGCCCCT TGTCCTCCTC TTGACCCTCC TTGGCAGCTC ACATGGAACA | 60 |
| 20 | GGGCCGGGTA TGACTTTGCA ACTGAAGCTG AAGGAGTCTT TTCTGACAAA TTCCTCCTAT | 120 |
| | GAGTCCAGCT TCCTGGAATT GCTTGAAAAG CTCTGCCTCC TCCTCCATCT CCCTTCAGGG | 180 |
| | ACCAGCGTCA CCCTCCACCA TGCAAGATCT CAACACCATG TTGTCTGCAA CACA | 234 |
| 25 | (2) INFORMATION FOR CEO ID NO. 27 | |
| 25 | (2) INFORMATION FOR SEQ ID NO: 27: (1) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 942 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 30 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| 35 | (B) CELL KIND: Stomach cancer | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

(D) CLONE NAME: HP10412

PCT/JP98/02445

| | ATGGTGGCGC | CTGTGTGGTA | CTTGGTAGCG | GCGGCTCTGC | TAGTCGGCTT | TATCCTCTTC | 6 |
|----|------------|------------|------------|------------|------------|------------|-----|
| | CTGACTCGCA | GCCGGGGCCG | GGCGGCATCA | GCCGGCCAAG | AGCCACTGCA | CAATGAGGAG | 120 |
| | CTGGCAGGAG | CAGGCCGGGT | GGCCCAGCCT | GGGCCCCTGG | AGCCTGAGGA | GCCGAGAGCT | 180 |
| • | GGAGGCAGGC | CTCGGCGCCG | GAGGGACCTG | GGCAGCCGCC | TACAGGCCCA | GCGTCGAGCC | 240 |
| 5 | CAGCGGGTGG | CCTGGGCAGA | AGCAGATGAG | AACGAGGAGG | AAGCTGTCAT | CCTAGCCCAG | 300 |
| | GAGGAGGAAG | GTGTCGAGAA | GCCAGCGGAA | ACTCACCTGT | CGGGGAAAAT | TGGAGCTAAG | 360 |
| | AAACTGCGGA | AGCTGGAGGA | GAAACAAGCG | CGAAAGGCCC | AGCGTGAGGC | AGAGGAGGCT | 420 |
| | GAACGTGAGG | AGCGGAAACG | ACTCGAGTCC | CAGCGCGAAG | CTGAGTGGAA | GAAGGAGGAG | 480 |
| | GAGCGGCTTC | GCCTGGAGGA | GGAGCAGAAG | GAGGAGGAGG | AGAGGAAGGC | CCGCGAGGAG | 540 |
| 10 | CAGGCCCAGC | GGGAGCATGA | GGAGTACCTG | AAACTGAAGG | AGGCCTTTGT | GGTGGAGGAG | 600 |
| | GAAGGCGTAG | GAGAGACCAT | GACTGAGGAA | CAGTCCCAGA | GCTTCCTGAC | AGAGTTCATC | 660 |
| | AACTACATCA | AGCAGTCCAA | GGTTGTGCTC | TTGGAAGACC | TGGCTTCCCA | GGTGGGCCTA | 720 |
| | CGCACTCAGG | ACACCATAAA | TCGCATCCAG | GACCTGCTGG | CTGAGGGGAC | TATAACAGGT | 780 |
| | GTGATTGACG | ACCGGGGCAA | GTTCATCTAC | ATAACCCCAG | AGGAACTGGC | CGCCGTGGCC | 840 |
| L5 | AACTTCATCC | GACAGCGGGG | CCGGGTGTCC | ATCGCCGAGC | TTGCCCAAGC | CAGCAACTCC | 900 |
| | CTCATCGCCT | GGGGCCGGGA | GTCCCCTGCC | CAAGCCCCAG | СС | | 942 |

(2) INFORMATION FOR SEQ ID NO: 28:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 585
- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- 25 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- 30 (D) CLONE NAME: HP10413

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

| | ATGGCTGCCG | AGGATGTGGT | GGCGACTGGC | GCCGACCCAA | GCGATCTGGA | GAGCGGCGGG | 60 |
|----|------------|------------|------------|------------|------------|------------|-----|
| 35 | CTGCTGCATG | AGATTTTCAC | GTCGCCGCTC | AACCTGCTGC | TGCTTGGCCT | CTGCATCTTC | 120 |
| | CTGCTCTACA | AGATCGTGCG | CGGGGACCAG | CCGGCGGCCA | GCGGCGACAG | CGACGACGAC | 180 |
| | GAGCCGCCCC | CTCTGCCCCG | CCTCAAGCGG | CGCGACTTCA | CCCCGCCGA | GCTGCGGCGC | 240 |
| | TTCGACGGCG | TCCAGGACCC | GCGCATACTC | ATGGCCATCA | ACGGCAAGGT | GTTCGATGTG | 300 |

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| | ACCAAAGGCC | GCAAATTCTA | CGGGCCCGAG | GGGCCGTATG | GGGTCTTTGC | TGGAAGAGAT | 360 |
|---|------------|------------|------------|------------|------------|------------|-----|
| | GCATCCAGGG | GCCTTGCCAC | ATTTTGCCTG | GATAAGGAAG | CACTGAAGGA | TGAGTACGAT | 420 |
| | GACCTTTCTG | ACCTCACTGC | TGCCCAGCAG | GAGACTCTGA | GTGACTGGGA | GTCTCAGTTC | 480 |
| | ACTTTCAAGT | ATCATCACGT | GGGCAAACTG | CTGAAGGAGG | GGGAGGAGCC | CACTGTGTAC | 540 |
| 5 | TCAGATGAGG | AAGAACCAAA | AGATGAGAGT | GCCCGGAAAA | ATGAT | | 585 |
| | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

10 (A

(A) LENGTH: 1386

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

15

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10415

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

| | ATGTTGGACT | TCGCGATCTT | CGCCGTTACC | TTCTTGCTGG | CGTTGGTGGG | AGCCGTGCTC | . 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| | TACCTCTATC | CGGCTTCCAG | ACAAGCTGCA | GGAATTCCAG | GGATTACTCC | AACTGAAGAA | 120 |
| 25 | AAAGATGGTA | ATCTTCCAGA | TATTGTGAAT | AGTGGAAGTT | TGCATGAGTT | CCTGGTTAAT | 180 |
| | TTGCATGAGA | GATATGGGCC | TGTGGTCTCC | TTCTGGTTTG | GCAGGCGCCT | CGTGGTTAGT | 240 |
| | TTGGGCACTG | TTGATGTACT | GAAGCAGCAT | ATCAATCCCA | ATAAGACATT | GGACCCTTTT | 300 |
| | GAAACCATGC | TGAAGTCATT | ATTAAGGTAT | CAATCTGGTG | GTGGCAGTGT | GAGTGAAAAC | 360 |
| | CACATGAGGA | AAAAATTGTA | TGAAAATGGT | GTGACTGATT | CTCTGAAGAG | TAACTTTGCC | 420 |
| 30 | CTCCTCCTAA | AGCTTTCAGA | AGAATTATTA | GATAAATGGC | TCTCCTACCC | AGAGACCCAG | 480 |
| | CACGTGCCCC | TCAGCCAGCA | TATGCTTGGT | TTTGCTATGA | AGTCTGTTAC | ACAGATGGTA | 540 |
| | ATGGGTAGTA | CATTTGAAGA | TGATCAGGAA | GTCATTCGCT | TCCAGAAGAA | TCATGGCACA | 600 |
| | GTTTGGTCTG | AGATTGGAAA | AGGCTTTCTA | GATGGGTCAC | TTGATAAAAA | CATGACTCGG | 660 |
| | AAAAAACAAT | ATGAAGATGC | CCTCATGCAA | CTGGAGTCTG | TTTTAAGGAA | CATCATAAAA | 720 |
| 35 | GAACGAAAAG | GAAGGAACTT | CAGTCAACAT | ATTTTCATTG | ACTCCTTAGT | ACAAGGGAAC | 780 |
| | CTTAATGACC | AACAGATCCT | AGAAGACAGT | ATGATATTTT | CTCTGGCCAG | TTGCATAATA | 840 |
| | ACTGCAAAAT | TGTGTACCTG | GGCAATCTGT | TTTTTAACCA | CCTCTGAAGA | AGTTCAAAAA | 900 |
| | AAATTATATG | AAGAGATAAA | CCAAGTTTTT | GGAAATGGTC | CTGTTACTCC | AGAGAAAATT | 960 |

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| GAGCAGCTCA | GATATTGTCA | GCATGTGCTT | TGTGAAACTG | TTCGAACTGC | CAAACTGACT | , 1020 |
|------------|------------|------------|------------|------------|------------|--------|
| CCAGTTTCTG | CCCAGCTTCA | AGATATTGAA | GGAAAAATTG | ACCGATTTAT | TATTCCTAGA | 1080 |
| GAGACCCTCG | TCCTTTATGC | CCTTGGTGTG | GTACTTCAGG | ATCCTAATAC | TTGGCCATCT | 1140 |
| CCACACAAGT | TTGATCCAGA | TCGGTTTGAT | GATGAATTAG | TAATGAAAAC | TTTTTCCTCA | 1200 |
| CTTGGATTCT | CAGGCACACA | GGAGTGTCCA | GAGTTGAGGT | TTGCATATAT | GGTGACCACA | 1260 |
| GTACTTCTTA | GTGTATTGGT | GAAGAGACTG | CACCTACTTT | CTGTGGAGGG | ACAGGTTATT | 1320 |
| GAAACAAAGT | ATGAACTGGT | AACATCATCA | AGGGAAGAAG | CTTGGATCAC | TGTCTCAAAG | 1380 |
| AGATAT | | | | | | 1386 |
| | | | | | | |

10

5

- (2) INFORMATION FOR SEQ ID NO: 30:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 741
 - (B) TYPE: Nucleic acid
- 15 (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

20

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP10419

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

25

| | | ATGGGGGCTG | CGGTGTTTTT | CGGCTGCACT | TTCGTCGCGT | TCGGCCCGGC | CTTCGCGCTT | 60 |
|---|----|------------|------------|------------|------------|------------|------------|-----|
| | | TTCTTGATCA | CTGTGGCTGG | GGACCCGCTT | CGCGTTATCA | TCCTGGTCGC | AGGGGCATTT | 120 |
| | | TTCTGGCTGG | TCTCCCTGCT | CCTGGCCTCT | GTGGTCTGGT | TCATCTTGGT | CCATGTGACC | 180 |
| | | GACCGGTCAG | ATGCCCGGCT | CCAGTACGGC | CTCCTGATTT | TTGGTGCTGC | TGTCTCTGTC | 240 |
| 3 | 30 | CTTCTACAGG | AGGTGTTCCG | CTTTGCCTAC | TACAAGCTGC | TTAAGAAGGC | AGATGAGGGG | 300 |
| | | TTAGCATCGC | TGAGTGAGGA | CGGAAGATCA | CCCATCTCCA | TCCGCCAGAT | GGCCTATGTT | 360 |
| | | TCTGGTCTCT | CCTTCGGTAT | CATCAGTGGT | GTCTTCTCTG | TTATCAATAT | TTTGGCTGAT | 420 |
| | | GCACTTGGGC | CAGGTGTGGT | TGGGATCCAT | GGAGACTCAC | CCTATTACTT | CCTGACTTCA | 480 |
| | | GCCTTTCTGA | CAGCAGCCAT | TATCCTGCTC | CATACCTTTT | GGGGAGTTGT | GTTCTTTGAT | 540 |
| 3 | 35 | GCCTGTGAGA | GGAGACGGTA | CTGGGCTTTG | GGCCTGGTGG | TTGGGAGTCA | CCTACTGACA | 600 |
| | | TCGGGACTGA | CATTCCTGAA | CCCCTGGTAT | GAGGCGAGCC | TGCTGCCCAT | CTATGCAGTC | 660 |
| | | ACTGTTTCCA | TGGGGCTCTG | GGCCTTCATC | ACAGCTGGAG | GGTCCCTCCG | AAGTATTCAG | 720 |
| | | CGCAGCCTCT | TGTGTAAGGA | С | • | | | 741 |

| | (2) INFORMATION FOR SEQ ID NO: 31: | |
|----|---|-----|
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 339 | |
| 5 | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | · | |
| 10 | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| | (B) CELL KIND: Stomach cancer | |
| | (D) CLONE NAME: HP10424 | |
| | | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31: | |
| | | |
| | ATGAACTTCT ATTTACTCCT AGCGAGCAGC ATTCTGTGTG CCTTGATTGT CTTCTGGAAA | 60 |
| | TATCGCCGCT TTCAGAGAAA CACTGGCGAA ATGTCATCAA ATTCAACTGC TCTTGCACTA | 120 |
| • | GTGAGACCCT CTTCTTCTGG GTTAATTAAC AGCAATACAG ACAACAATCT TGCAGTCTAC | 180 |
| 20 | GACCTCTCTC GGGATATTTT AAATAATTTC CCACACTCAA TAGCCAGGCA GAAGCGAATA | 240 |
| | TTGGTAAACC TCAGTATGGT GGAAAACAAG CTGGTTGAAC TGGAACATAC TCTACTTAGC | 300 |
| | AAGGGTTTCA GAGGTGCATC ACCTCACCGG AAATCCACC | 339 |
| | | |
| 25 | (2) INFORMATION FOR SEQ ID NO: 32: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 1095 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 30 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | | |
| • | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |

(B) CELL KIND: Epidermoid carcinoma

(C) CELL LINE: KB

(D) CLONE NAME: HP10428

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

| • | ATGGGGAGGT | GGGCCCTCGA | TGTGGCCTTT | TTGTGGAAGG | CGGTGTTGAC | CCTGGGGCTG | 60 |
|----|------------|------------|------------|------------|------------|------------|------|
| | GTGCTTCTCT | ACTACTGCTT | CTCCATCGGC | ATCACCTTCT | ACAACAAGTG | GCTGACAAAG | 120 |
| 5 | AGCTTCCATT | TCCCCCTCTT | CATGACGATG | CTGCACCTGG | CCGTGATCTT | CCTCTTCTCC | 180 |
| | GCCCTGTCCA | GGGCGCTGGT | TCAGTGCTCC | AGCCACAGGG | CCCGTGTGGT | GCTGAGCTGG | 240 |
| | GCCGACTACC | TCAGAAGAGT | GGCTCCCACA | GCTCTGGCGA | CGGCGCTTGA | CGTGGGCTTG | 300 |
| | TCCAACTGGA | GCTTCCTGTA | TGTCACCGTC | TCGCTGTACA | CAATGACCAA | ATCCTCAGCT | 360 |
| | GTCCTCTTCA | TCTTGATCTT | CTCTCTGATC | TTCAAGCTGG | AGGAGCTGCG | CGCGGCACTG | 420 |
| 10 | GTCCTGGTGG | TCCTCCTCAT | CGCCGGGGGT | CTCTTCATGT | TCACCTACAA | GTCCACACAG | 480 |
| | TTCAACGTGG | AGGGCTTCGC | CTTGGTGCTG | GGGGCCTCGT | TCATCGGTGG | CATTCGCTGG | 540 |
| • | ACCCTCACCC | AGATGCTCCT | GCAGAAGGCT | GAACTCGGCC | TCCAGAATCC | CATCGACACC | 600 |
| | ATGTTCCACC | TGCAGCCACT | CATGTTCCTG | GGGCTCTTCC | CTCTCTTTGC | TGTATTTGAA | 660 |
| | GGTCTCCATT | TGTCCACATC | TGAGAAAATC | TTCCGTTTCC | AGGACACAGG | GCTGCTCCTG | 720 |
| 15 | CGGGTACTTG | GGAGCCTCTT | CCTTGGCGGG | ATTCTCGCCT | TTGGTTTGGG | CTTCTCTGAG | 780 |
| | TTCCTCCTGG | TCTCCAGAAC | CTCCAGCCTC | ACTCTCTCCA | TTGCCGGCAT | TTTTAAGGAA | 840 |
| | GTCTGCACTT | TGCTGTTGGC | AGCTCATCTG | CTGGGCGATC | AGATCAGCCT | CCTGAACTGG | 900 |
| | CTGGGCTTCG | CCCTCTGCCT | CTCGGGAATA | TCCCTCCACG | TTGCCCTCAA | AGCCCTGCAT | 960 |
| | TCCAGAGGTG | ATGGTGGCCC | CAAGGCCTTG | AAGGGGCTGG | GCTCCAGCCC | CGACCTGGAG | 1020 |
| 20 | CTGCTGCTCC | GGAGCAGCCA | GCGGGAGGAA | GGTGACAATG | AGGAGGAGGA | GTACTTTGTG | 1080 |
| | GCCCAGGGGC | AGCAG | | | | | 1095 |

(2) INFORMATION FOR SEQ ID NO: 33:

- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 678
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
- 30 (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
- 35 (D) CLONE NAME: HP10429
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

117

| | 117 | |
|----|---|-----|
| | ATGCCTACCA CAAAGAAGAC ATTGATGTTC TTATCAAGCT TTTTCACCAG CCTTGGGTCC | 60 |
| | TTCATTGTAA TTTGCTCTAT TCTTGGGACA CAAGCATGGA TCACCAGTAC AATTGCTGTT | 120 |
| | AGAGACTCTG CTTCAAATGG GAGCATTTTC ATCACTTACG GACTTTTTCG TGGGGAGAGT | 180 |
| | AGTGAAGAAT TGAGTCACGG ACTTGCAGAA CCAAAGAAAA AGTTTGCAGT TTTAGAGATA | 240 |
| 5 | CTGAATAATT CTTCCCAAAA AACTCTGCAT TCGGTGACTA TCCTGTTCCT GGTCCTGAGT | 300 |
| | TTGATCACGT CGCTGCTGAG CTCTGGGTTT ACCTTCTACA ACAGCATCAG CAACCCTTAC | 360 |
| | CAGACATTCC TGGGGCCGAC GGGGGTGTAC ACCTGGAACG GGCTCGGTGC ATCCTTCGTT | 420 |
| | TTTGTGACCA TGATACTGTT TGTGGCGAAC ACGCAGTCCA ACCAACTCTC CGAAGAGTTG | 480 |
| | TTCCAAATGC TTTACCCGGC AACCACCAGT AAAGGAACGA CCCACAGTTA CGGATACTCG | 540 |
| 10 | TTCTGGCTCA TACTGCTCGT CATTCTTCTA AATATAGTCA CTGTAACCAT CATCATTTTC | 600 |
| | TACCAGAAGG CCAGATACCA GCGGAAGCAG GAGCAGAGAA AGCCAATGGA ATATGCTCCA | 660 |
| | AGGGACGGAA TTTTATTC | 678 |
| | | |
| | | |
| 15 | (2) INFORMATION FOR SEQ ID NO: 34: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 387 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 20 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | | |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| 25 | (B) CELL KIND: Liver | |
| | (D) CLONE NAME: HP10432 | |
| | | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34: | |
| | | |
| 30 | | |
| | ATGGCTCGGG GCTCGCTGCG CCGGTTGCTG CGGCTCCTCG TGCTGGGGGCT CTGGCTGG | 60 |
| | TTGCTGCGCT CCGTGGCCGG GGAGCAAGCG CCAGGCACCG CCCCCTGCTC CCGCGGCAGC | 120 |
| | TCCTGGAGCG CGGACCTGGA CAAGTGCATG GACTGCGCGT CTTGCAGGGC GCGACCGCAC | 180 |
| | AGCGACTTCT GCCTGGGCTG CGCTGCAGCA CCTCCTGCCC CCTTCCGGCT GCTTTGGCCC | 240 |
| 35 | ATCCTTGGGG GCGCTCTGAG CCTGACCTTC GTGCTGGGGC TGCTTTCTGG CTTTTTGGTC | 300 |
| | TGGAGACGAT GCCGCAGGAG AGAGAAGTTC ACCACCCCCA TAGAGGAGAC CGGCGGAGAG | 360 |
| | GGCTGCCCAG CTGTGGCGCT GATCCAG | 387 |

WO 98/55508

| | (2) INFORM | ATION FOR SEQ ID NO: 35: | |
|----|------------|--|-----|
| | (i) | SEQUENCE CHARACTERISTICS: | |
| | | (A) LENGTH: 489 | |
| | | (B) TYPE: Nucleic acid | |
| 5 | | (C) STRANDEDNESS: Double | |
| | | (D) TOPOLOGY: Linear | |
| | (ii) | SEQUENCE KIND: cDNA to mRNA | |
| | | | |
| 10 | (V1) | ORIGINAL SOURCE: | |
| 10 | | (A) ORGANISM: Homo sapiens | • |
| | | (B) CELL KIND: Liver | |
| | | (D) CLONE NAME: HP10433 | |
| | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO: 35: | |
| 15 | (2) | Dagonion productive. Buy in No. 33. | |
| | ATGCGACGGC | TGCTGATCCC TCTGGCCCTG TGGCTGGGCG CGGTGGGCGT GGGCGTCGCC | 60 |
| | | AAGCCCAGCG CCGGGGCCTG CAGGTGGCCC TGGAGGAATT TCACAAGCAC | 120 |
| | | AGTGGGCCTT CCAGGAGACC AGTGTGGAGA GCGCCGTGGA CACGCCCTTC | 180 |
| | CCAGCTGGAA | TATTTGTGAG GCTGGAATTT AAGCTGCAGC AGACAAGCTG CCGGAAGAGG | 240 |
| 20 | GACTGGAAGA | AACCCGAGTG CAAAGTCAGG CCCAATGGGA GGAAACGGAA ATGCCTGGCC | 300 |
| | TGCATCAAAC | TGGGCTCTGA GGACAAAGTT CTGGGCCGGT TGGTCCACTG CCCCATAGAG | 360 |
| | ACCCAAGTTC | TGCGGGAGGC TGAGGAGCAC CAGGAGACCC AGTGCCTCAG GGTGCAGCGG | 420 |
| | GCTGGTGAGG | ACCCCCACAG CTTCTACTTC CCTGGACAGT TCGCCTTCTC CAAGGCCCTG | 480 |
| | CCCCGCAGC | | 489 |
| 25 | | | |
| | | | |
| | | TION FOR SEQ ID NO: 36: | |
| | (i) S | EQUENCE CHARACTERISTICS: | |
| 20 | | (A) LENGTH: 579 | |
| 30 | | (B) TYPE: Nucleic acid | |
| | | (C) STRANDEDNESS: Double | |
| | | (D) TOPOLOGY: Linear | |
| | (11) | SEQUENCE KIND: cDNA to mRNA | |
| 35 | (vi) | ORIGINAL SOURCE: | |
| | | (A) ORGANISM: Homo sapiens | |
| | | (B) CELL KIND: Stomach cancer | |
| | | (D) CLONE NAME: HP10480 | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

| | ATGATCCGCT GCGGCCTGGC CTGCGAGCGC TGCCGCTGGA TCCTGCCCCT GCTCCTACTC | 6 |
|-----|---|-----|
| | AGCGCCATCG CCTTCGACAT CATCGCGCTG GCCGGCCGCG GCTGGTTGCA GTCTAGCGAC | 12 |
| 5 | CACGGCCAGA CGTCCTCGCT GTGGTGGAAA TGCTCCCAAG AGGGCGGCGG CAGCGGGTCC | 18 |
| | TACGAGGAGG GCTGTCAGAG CCTCATGGAG TACGCGTGGG GTAGAGCAGC GGCTGCCATG | 24 |
| | CTCTTCTGTG GCTTCATCAT CCTGGTGATC TGTTTCATCC TCTCCTTCTT CGCCCTCTGT | 30 |
| | GGACCCCAGA TGCTTGTCTT CCTGAGAGTG ATTGGAGGTC TCCTTGCCTT GGCTGCTGTG | 36 |
| | TTCCAGATCA TCTCCCTGGT AATTTACCCC GTGAAGTACA CCCAGACCTT CACCCTTCAT | 42 |
| 10 | GCCAACCGTG CTGTCACTTA CATCTATAAC TGGGCCTACG GCTTTGGGTG GGCAGCCACG | 48 |
| | ATTATCCTGA TCGGCTGTGC CTTCTTCTTC TGCTGCCTCC CCAACTACGA AGATGACCTT | 54 |
| | CTGGGCAATG CCAAGCCCAG GTACTTCTAC ACATCTGCC | 57 |
| | | |
| | | |
| 15 | (2) INFORMATION FOR SEQ ID NO: 37: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 1502 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 20 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | · | |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| 25 | (B) CELL KIND: Liver | |
| | (D) CLONE NAME: HP01263 | |
| | (to) aparenar and areas | |
| | (ix) SEQUENCE CHARACTERISTICS: | |
| 20 | (A) CHARACTERIZATION CODE: CDS | |
| 30 | (B) EXISTENCE POSITION: 37 1185 | |
| | (C) CHARACTERIZATION METHOD: E | |
| | (with CEGUENCE DECOMEDATION OF THE AS | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37: | |
| 35 | ACAAACTGAC CCATCCTGGG CCTTGTTCTC CACAGA ATG GGT CTG CTC CTT CCC | ٠, |
| J J | | 54 |
| | Met Gly Leu Leu Pro 1 5 | |
| | CTC CCA CTC TCC ATC CTA CTC CTC TCC TCC | 100 |

| | Leu | Ala | Leu | Cys | Ile | Leu | Val | Leu | Cys | Cys | Gly | Ala | Met | Sei | Pro | Pro | |
|----|-------|-----|-----|------|--------------|------|-----|------------|---------|---------|-----|-------|-------------|-------|------------|---------|-----|
| | | | | 10 |) | | | | 15 | , | | | | 20 |) | | |
| | CAG | CTG | GCC | CTC | AAC | ccc | TCG | GCT | CTG | CTC | TCC | CGG | GGC | TGC | TAA : | GAC | 150 |
| | Gln | Leu | Ala | Leu | Asn | Pro | Ser | Ala | Leu | Leu | Ser | Arg | Gly | Cys | Asn | Asp | |
| 5 | | | 25 | | | | | 30 | | | | | 35 | , | | | |
| | TCC | GAT | GTG | CTG | GCA | GTT | GCA | GGC | TTT | GCC | CTG | CGG | GAT | ' ATI | AAC | AAA | 198 |
| | Ser | Asp | Val | Leu | Ala | Val | Ala | Gly | Phe | Ala | Leu | Arg | Asp | Ile | Asn | Lys | |
| | | 40 | | | | | 45 | | | | | 50 | ı | | | | |
| | GAC | AGA | AAG | GAT | GGC | TAT | GTG | CTG | AGA | CTC | AAC | CGA | GTG | AAC | GAC | GCC | 246 |
| 10 | Asp | Arg | Lys | Asp | Gly | Tyr | Va1 | Leu | Arg | Leu | Asn | Arg | Val | Asn | Asp | Ala | |
| | 55 | | | | | 60 | | | | | 65 | | | | | 70 | |
| | CAG | GAA | TAC | AGA | CGG | GGT | GGC | CTG | GGA | TCT | CTG | TTC | TAT | CTT | ACA | CTG | 294 |
| | Gln | Glu | Tyr | Arg | Arg | Gly | Gly | Leu | Gly | Ser | Leu | Phe | Tyr | Leu | Thr | Leu | |
| | | | | | 75 | | | | | 80 | | | | | 85 | | • |
| 15 | GAT | GTG | CTA | GAG | ACT | GAC | TGC | CAT | GTG | CTC | AGA | AAG | AAG | GCA | TGG | CAA | 342 |
| | Asp | Val | Leu | Glu | Thr | Asp | Cys | His | Val | Leu | Arg | Lys | Lys | Ala | Trp | Gln | |
| | | | | 90 | | | | | 95 | | | | | 100 | | | |
| | | | | | * | • | | | | | | | | | TGC | | 390 |
| | Asp | Cys | Gly | Met | Arg | Ile | Phe | Phe | Glu | Ser | Val | Tyr | Gly | Gln | Cys | Lys | |
| 20 | | | 105 | | | | | 110 | | | | | 115 | | | | |
| | | | | | | | | | | | | | | | GCT | | 438 |
| | Ala | | Phe | Tyr | Met | Asn | | Pro | Ser | Arg | Val | Leu | Tyr | Leu | Ala | Ala | |
| | m . m | 120 | | | | | 125 | | | | | 130 | | | | | |
| 25 | | | | | | | * | | | | | | | | ATG | | 486 |
| 25 | | Asn | Cys | Tnr | Leu | | Pro | Val | Ser | Lys | | Lys | Ile | Tyr | Met | | |
| | 135 | 00m | ~ ~ | ma a | 201 | 140 | | | | | 145 | | | | | 150 | |
| | | | | | | | | | | | | | | | CAC | | 534 |
| | Cys | FIO | wsb | cys | 155 | ser | ser | TIE | Pro | | Asp | Ser | Ser | Asn | His | GIn | |
| 30 | ara | СТС | GAG | ርርጥ | | ۸۵۵ | CAC | TO TO | C TI TI | 160 | | m.c | 440 | 4 4 M | 165 | 440 | 500 |
| 50 | | | | | | | | | | | | | | | GAG Glu | | 582 |
| | *** | Dea | O1u | 170 | nia | 1111 | GIU | ser | 175 | MIG | гая | Tyr | ASII | 180 | GIU | Asn | |
| | ACA | TCC | AAG | | ТАТ | тст | СТС | ጥፐር | | GTC | ۸۵۵ | AGG. | ር ር ፓ | | AGC | CAG | 630 |
| | | | | | | | | | | | | | | | Ser | | 030 |
| 35 | | | 185 | | - , - | | | 190 | -, - | · · · · | | ··- 5 | 195 | JU1 | JC1 | V + 4.1 | |
| | TGG | GTG | | GGC | CCT | TCT | TAC | | GTG | GAA | TAC | ТТА | | AAA | GAA | TCA | 678 |
| | | | | | | | | | | | | | | | Glu | | 0.0 |
| | • | 200 | | • | _ | | 205 | | | | | 210 | | -, - | - | | |

| | CCA | TGI | ACT | AAA | TCC | CAG | GCC | AGC | AGC | TGT | TCA | CTT | CAG | TCC | TCC | GAC | 726 |
|----|-----|-------|-----|-----------------|---------------|---------|--------|-------|--------|--------|-------|------|-------|-------|-------|--------|------|
| | Pro | Cys | Thr | Lys | Ser | Gln | Ala | Ser | Ser | Cys | Ser | Leu | Gln | Ser | Ser | Asp | |
| | 215 | | | | | 220 | | | | | 225 | | | | | 230 | |
| | TCT | GTG | CCT | GTT | GGT | CTT | TGC | AAA | GGT | TCT | CTG | ACT | CGA | ACA | CAC | TGG | 774 |
| 5 | Ser | Val | Pro | Val | Gly | Leu | Cys | Lys | G1y | Ser | Leu | Thr | Arg | Thr | His | Trp | |
| | | | | | 235 | | | | | 240 | | | | | 245 | | |
| | GAA | AAG | TTT | GTC | TCT | GTG | ACT | TGT | GAC | TTC | TTT | GAA | TCA | CAG | GCT | CCA | 822 |
| | Glu | Lys | Phe | Val | Ser | Val | Thr | Сув | Asp | Phe | Phe | Glu | Ser | Gln | Ala | Pro | |
| • | | | | 250 | | | | | 255 | | | | | 260 | | | |
| 10 | GCC | ACT | GGA | AGT | GAA | AAC | TCT | GCT | GTT | AAC | CAG | AAA | CCT | ACA | AAC | CTT | 870 |
| | Ala | Thr | Gly | Ser | Glu | Asn | Ser | Ala | Val | Asn | Gln | Lys | Pro | Thr | Asn | Leu | |
| • | | | 265 | | | | | 270 | | | | | 275 | | | | |
| | CCC | AAG | GTG | GAA | GAA | TCC | CAG | CAG | AAA | AAC | ACC | CCC | CCA | ACA | GAC | TCC | 918 |
| | Pro | Lys | Val | Glu | Glu | Ser | Gln | Gln | Lys | Asn | Thr | Pro | Pro | Thr | Asp | Ser | |
| 15 | | 280 | | | | | 285 | | | | | 290 | | | | | |
| | | | AAA | | | | | | | | | | | | | | 966 |
| | | Ser | Lys | Ala | Gly | Pro | Arg | Gly | Ser | Val | Gln | Tyr | Leu | Pro | Asp | Leu | |
| | 295 | | | | | 300 | | | | | 305 | | | | | 310 | |
| | | | AAA | | | | | | | | | | | | | | 1014 |
| 20 | Asp | Asp | Lys | Asn | Ser | Gln | Glu | Lys | Gly | Pro | Gln | Glu | Ala | Phe | Pro | Val | |
| | | | | | 315 | | | | | 320 | | | | | 325 | | |
| | | | GAC | | | | | | | | | | | | | | 1062 |
| | His | Leu | Asp | | Thr | Thr | Asn | Pro | Gln | Gly | Glu | Thr | Leu | Asp | Ile | Ser | |
| 25 | | | | 330 | | | | | 335 | | | | | 340 | | | |
| 25 | | | TTC | | | | | | | | | | | | | | 1110 |
| | Pne | Leu | Phe | Leu | Glu | Pro | Met | | Glu | Lys | Leu | Val | | Leu | Pro | Phe | |
| | ccc | A A A | 345 | | | 000 | 400 | 350 | 242 | | | | 355 | | | | |
| | | | GAA | | | | | | | | | | | | | | 1158 |
| 30 | 110 | 360 | Glu | Lys | WIR | Arg | | AIB | GIU | Cys | | | Pro | AIA | GIn . | Asn | |
| 30 | GCC | | CCT | ር ጥጥ | C T C | C TO TO | 365 | 004 | ma . a | | | 370 | | m | 0.00 | 00 | 1010 |
| | | | Pro | | | | | | IGAG | AATC | AU A | CAGA | GTCT | T CT | GTAG | 66 | 1210 |
| | 375 | 501 | 110 | Leu | VAI | 380 | PIO | PIO | | | | | | | | | |
| | | ССТС | :CG | CGCA | ምር ል ሶ | | GG & C | GCC 4 | ምረረ | CC A C | ርልጥ ፡ | 0040 | AC AC | A C A | 2400 | GTGCA | 1070 |
| 35 | | | | | | | | | | | | | | | | TGACT | |
| | | | | | | | | | | | | | | | | ACTGC | |
| | | | | | | | | | | | | | | | | ATGCC | • |
| | | | | | | | | | | | | | TCAG | | | .11000 | 1502 |

| | (2) INFO | RMATION | FOR SEQ | ID NO: | 38: | | | | | |
|----|-----------|-----------|-----------|----------|--------|--------|---------|-----------|--------|-----|
| | (i |) SEQUE | NCE CHAR | ACTERIST | CICS: | | | | | |
| | | (A) | LENGTH: | 1349 | | | | | | |
| 5 | | (B) | TYPE: N | ucleic a | cid | | | | | |
| | | (C) | STRANDE | DNESS: D | ouble | | | | | |
| | | (D) | TOPOLOG | Y: Linea | r | | | | | |
| | (i | i) SEQUI | ENCE KIN | D: cDNA | to mRN | Α | | • | | |
| | | | | | | | | | | |
| 10 | (v | i) ORIG | INAL SOU | RCE: | | | | | | |
| | | (A) | ORGANIS | 1: Homo | sapien | s | | | | |
| | | (B) | CELL KI | ND: Live | r | | | | | |
| | | (D) | CLONE NA | AME: HPO | 1299 | | | | | |
| | | | | | | | | | | |
| 15 | | | | | | | | | | |
| | (i: | x) SEQUE | ENCE CHAP | RACTERIS | TICS: | | | | | |
| | | (A) | CHARACTI | ERIZATIO | N CODE | : CDS | | | | |
| | | ·(B) | EXISTENC | E POSIT | ION: 1 | 11 1 | 064 | | • | |
| | | (C) | CHARACTE | ERIZATIO | N METH | OD: E | | | | |
| 20 | | | | | • | | | | | |
| | (x. | i) SEQUE | ENCE DESC | RIPTION | : SEQ | ID NO: | 38: | | | |
| | | | | | | | | | | |
| | AGCAGTTG | GG GCAGG | AGGAA GC | CGACTGC | T GCCT | GGTCTG | CAAAGA | AGTC CTT | CAAGTC | 60 |
| | TCTAGGAC' | IG GACTO | TTCCT AA | GCAAGTC | C GAGA | AGGAAG | CACCCT | CACT ATG | TGG | 116 |
| 25 | | | | | | | | Met | Trp | |
| | | | | | | | | 1 | | |
| | | CTG GCG | GCC TTC | GTG GGC | CTG TA | AC TAC | CTT CT | G CAC TGG | TAC | |
| | 164 | | | | | | | | | |
| | Leu Tyr I | | Ala Phe | Val Gly | Leu Ty | r Tyr | Leu Le | u His Trp | Tyr | |
| 30 | | 5 | | 10 | | | 13 | | | |
| | CGG GAG A | | | | | | | | | 212 |
| | Arg Glu A | Arg Gln | Val Val | Ser His | Leu Gl | ln Asp | Lys Ty | r Val Phe | Ile | |
| | 20 | | | 25 | | | 30 | | | |
| | ACG GGC 1 | | | | | | | | | 260 |
| 35 | Thr Gly (| Cys Asp | | Phe Gly | Asn Le | | Ala Arg | g Gln Leu | 7 | |
| | 35 | | 40 | | | 45 | | | 50 | |
| | GCA CGA G | | | | | | | | | 308 |
| | Ala Arg G | ily Leu . | Arg Val | Leu Ala | Ala Cv | s Len | Thr Gli | ı Lvs Glv | Ala | |

| | | | | | | 55 | 5 | | | | 60 |) | | | | 6. | 5 | |
|---|----|------------|-------------|-------|-------|-------|-------|-------|-----|-------|-------|----------|-------|-----|-----|-----|-----|-----|
| | | GAG | CAG | CTO | AGG | GGC | CAG | ACC | TC | GA(| AGO | CTO | GAG | ACC | GTO | ACC | CTG | 356 |
| | | Glu | Glr | ı Lev | ı Arg | Gly | Glr | Thr | Sei | : Asp | Arg | g Lei | ı Glu | Thr | Va] | Thi | Leu | |
| | | | | | 70 |) | | | | 75 | 5 | | | | 80 |) | | |
| | 5 | GAT | GTI | ACC | AAG | ATG | GAG | AGC | ATC | GCI | GCA | GCI | CACI | CAG | TGG | GTO | AAG | 404 |
| | | Asp | Val | . Thr | Lys | Met | Glu | Ser | Ile | Ala | Ala | Ala | Thr | Gln | Trp | Va] | Lys | |
| | | | | ∙85 | • | | | | 90 |) | | | | 95 | , | | | |
| | | GAG | CAT | GTG | GGG | GAC | AGA | GGA | CTC | TGG | GGA | CTG | GTG | AAC | AAT | GCA | GGC | 452 |
| | | Glu | His | Val | Gly | Asp | Arg | Gly | Leu | Trp | Gly | Leu | Val | Asn | Asn | Ala | Gly | |
| | 10 | | 100 |) | | | | 105 | | | | | 110 | | | | | |
| | | ATT | CTT | ACA | CCA | ATT | ACC | TTA | TGT | GAG | TGG | CTG | AAC | ACT | GAG | GAC | TCT | 500 |
| | | Ile | Leu | Thr | Pro | Ile | Thr | Leu | Cys | Glu | Trp | Leu | Asn | Thr | Glu | Asp | Ser | |
| - | | 115 | | | | | 120 | | | | | 125 | | | | | 130 | |
| | | ATG | AAT | ATG | CTC | AAA | GTG | AAC | CTC | ATT | GGT | GTG | ATC | CAG | GTG | ACC | TTG | 548 |
| | 15 | Met | Asn | Met | Leu | Lys | Val | Asn | Leu | Ile | Gly | Val | Ile | Gln | Val | Thr | Leu | |
| | | | | | | 135 | | | | | 140 | | | | | 145 | | |
| | | AGC | ATG | CTT | CCT | TTG | GTG | AGG | AGA | GCA | CGG | GGA | AGA | ATT | GTC | AAT | GTC | 596 |
| | | Ser | Met | Leu | Pro | Leu | Val | Arg | Arg | Ala | Arg | Gly | Arg | Ile | Val | Asn | Val | |
| | | | | | 150 | | | | | 155 | | | | | 160 | | | |
| | 20 | | | | | | AGA | | | | | | | | | | | 644 |
| | | Ser | Ser | | Leu | Gly | Arg | Val | Ala | Phe | Phe | Va1 | Gly | Gly | Tyr | Cys | Val | |
| | | | | 165 | | | | | 170 | | | | | 175 | | | | |
| | | | | | | | GAA | | | | | | | | | | | 692 |
| | | Ser | | Tyr | Gly | Val | Glu | Ala | Phe | Ser | Asp | Ile | Leu | Arg | Arg | Glu | Ile | |
| | 25 | | 180 | | | | | 185 | | | | | 190 | | | | | |
| | | | | | | | AAA | | | | | | | | | | | 740 |
| | | | His | Phe | Gly | Val | Lys | Ile | Ser | Ile | Val | Glu | Pro | Gly | Tyr | Phe | Arg | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | 210 | |
| | 20 | | | | | | ATG | | | | | | | | | | | 788 |
| | 30 | Thr | Gly | Met | Thr | | Met | Thr | Gln | Ser | | Glu | Arg | Met | Lys | Gln | Ser | |
| | | 500 | | | | 215 | | | | | 220 | | | | | 225 | | |
| | | | | | | | AAG | | | | | | | | | | | 836 |
| | | Trp | Lys | Glu | | Pro | Lys | His | Ile | | Glu | Thr | Tyr | | | Gln | Tyr | |
| | 35 | արար | CATE | 000 | 230 | m 4 0 | 4 4 M | 4.50 | | 235 | | | | | 240 | | | |
| | | | | | | | TAA | | | | | | | | | | | 884 |
| | | - 116 | voh | 245 | Leu | TYE | Asn | тте | | гàг | GIU | GIÀ | | | ASN | cys | ser | |
| | | ACA | AA C | | A A C | ርጥር | CTC | A C/M | 250 | mcc. | 4 m.c | . | | 255 | 055 | | maa | |
| | | ACA | W | 010 | nnu | 010 | GIC | AUT | GAU | IGU | AIG | GAA | CAT | GCT | CTG | AUA | TUG | 932 |

124

| | Thr | Asn | Leu | Asn | Leu | Val | Thr | Asp | Cys | Met | Glu | His | Ala | Leu | Thr | Ser | |
|----|------|-------|------|----------|------|---------|-------------|-------|------|-------|-----|------|-------|-------|------|----------------|--------------|
| | | 260 | | | | | 265 | | | | | 270 | | | | | |
| | | | | | | | | | | | | | GCT | | | | 980 |
| _ | | His | Pro | Arg | Thr | | Tyr | Ser | Ala | Gly | Trp | Asp | Ala | Lys | Phe | Phe | |
| 5 | 275 | | | | | 280 | | | | | 285 | | | | | 290 | |
| | | | | | | | | | | | | | GAC | | | | 1028 |
| | Phe | Ile | Pro | Leu | | Tyr | Leu | Pro | Thr | | Leu | Ala | Asp | Tyr | | Leu | |
| | 4.05 | | | 500 | 295 | | | | | 300 | | | | | 305 | | |
| 10 | | | | | | | | | | | | TAAA | AGAAA | AAC 1 | rggg | TGGT | 1080 |
| 10 | rnr | Arg | ser | Trp | Pro | Lys | Pro | Ala | | Ala | Val | | | | | | |
| | CCMM | omme. | | 310 | | | | | 315 | | | | | | | | |
| | | | | | | | | | | | | | | | | TTAGA | |
| | | | | | | | | | | | | | | | | ATCAG | |
| 15 | | | | | | | | | | | | | | | | TCTTT TGCCT | |
| 13 | TATT | | | | | | | | 1116 | ,101A | MAG | IGAF | IICAI | .11 6 | 1101 | IGCCI | 1320 1349 |
| | | | | .0 .11.0 | | 711 IM: | MIOIN | 1111 | | | | | | | • | | 1349 |
| | | | | | | | | | | | | | | | | | |
| | (2) | INFO | RMAT | ON | FOR | SEQ | ID N | 10: 3 | 9: | | | | | | | | |
| 20 | | (i |) SE | QUEN | CE C | HARA | CTER | ISTI | CS: | | | | | | | | |
| | | | | (A) | LENG | TH: | 1643 | 3 | | | | | | | | | |
| | | | | (B) | TYPE | : Nu | clei | .c ac | id | | | | | | | | |
| | | | | (C) | STRA | NDED | NESS | : Do | uble | | | | | | | | |
| | | | | (D) | TOPO | LOGY | : Li | near | | | | | | | | | |
| 25 | | (i | i) S | EQUE | NCE | KIND | : cD | NA t | o mR | NA | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | (v | i) 0 | RIGI | NAL | SOUR | CE: | | | | | | | | | | |
| | | | | (A) | ORGA | NISM | : <i>Ho</i> | mo s | apie | ns | | | | | | | |
| | | | | (B) | CELL | KIN | D: L | iver | | | | | | | | | |
| 30 | | | | (D) | CLON | E NA | ME: | HP01 | 347 | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | (i: | | EQUE | | | | | | | | | | | | | |
| | | | | (A) | | | | | | | | | | | | | |
| 25 | | | | (B) | | | | | | | | | | | | | |
| 35 | | | | (C) | CHAR | ACTE | RIZA | TION | MET | HOD: | E | | | | | | |
| | | | | | | | | | | | | | | | | | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

| | AAC | ATCI | GGG | GACA | .GCGG | GA A | AAC | ATG | AGT | GAC | TCC | AAG | GAA | CCA | AGG | GTG | 51 |
|----|-----|------|-----|------|-------|------|-----|-----|-----|-----|-----|------|-----|-----|-------|-----|-----|
| | | | | | | | | Met | Ser | Asp | Ser | Lys | Glu | Pro | Arg | Val | • |
| | | • | | • | | | | 1 | | | | 5 | | | | | |
| | CAG | CAG | CTG | GGC | CTC | CTG | GGG | TGT | CTI | GGC | CAT | GGC | GCC | CTG | GTO | CTG | 99 |
| 5 | Gln | Gln | Leu | Gly | Leu | Leu | Gly | Cys | Leu | Gly | His | Gly | Ala | Let | ı Val | Leu | |
| | 10 | | | | | 15 | | | | | 20 |) | | | | 25 | |
| | CAA | CTC | CTC | TCC | TTC | ATG | CTC | TTG | GCT | GGG | GTC | CTG | GTG | GCC | ATC | CTT | 147 |
| | Gln | Leu | Leu | Ser | Phe | Met | Leu | Leu | Ala | Gly | Val | Leu | Val | Ala | Ile | Leu | |
| | | • | | | 30 | | | | | 35 | | | | | 40 |) | |
| 10 | GTC | CAA | GTG | TCC | AAG | GTC | ccc | AGC | TCC | CTA | AGT | CAG | GAA | CAA | TCC | GAG | 195 |
| | Val | Gln | Va1 | Ser | Lys | Val | Pro | Ser | Ser | Leu | Ser | Gln | Glu | Gln | Ser | Glu | |
| | | | | 45 | | | | , | 50 | | | | | 55 | | | |
| | CAA | GAC | GCA | ATC | TAC | CAG | AAC | CTG | ACC | CAG | CTT | AAA | GCT | GCA | GTG | GGT | 243 |
| | Gln | Asp | Ala | Ile | Tyr | Gln | Asn | Leu | Thr | Gln | Leu | Lys | Ala | Ala | Val | Gly | |
| 15 | | | 60 | | | | | 65 | | | | | 70 | | | | |
| | GAG | CTC | TCA | GAG | AAA | TCC | AAG | CTG | CAG | GAG | ATC | TAC | CAG | GAG | CTG | ACC | 291 |
| | G1u | Leu | Ser | Glu | Lys | Ser | Lys | Leu | Gln | Glu | Ile | Tyr | Gln | Glu | Leu | Thr | |
| | | 75 | | | | | 80 | | | | | 85 | | | | | |
| | CAG | CTG | AAG | GCT | GCA | GTG | GGT | GAG | TTG | CCA | GAG | AAA | TCC | AAG | CTG | CAG | 339 |
| 20 | Gln | Leu | Lys | Ala | Ala | Val | Gly | Glu | Leu | Pro | Glu | Lys | Ser | Lys | Leu | Gln | |
| | 90 | | | | | 95 | | | | | 100 | | | | | 105 | |
| | GAG | ATC | TAC | CAG | GAG | CTG | ACC | CGG | CTG | AAG | GCT | GCA | GTG | GGT | GAG | TTG | 387 |
| | Glu | Ile | Tyr | Gln | Glu | Leu | Thr | Arg | Leu | Lys | Ala | -Ala | Val | Gly | Glu | Leu | |
| | | | | | 110 | | | | | 115 | | | | | 120 | | |
| 25 | CCA | GAG | AAA | TCC | AAG | CTG | CAG | GAG | ATC | TAC | CAG | GAG | CTG | ACC | CGG | CTG | 435 |
| | Pro | Glu | Lys | Ser | Lys | Leu | Gln | Glu | Ile | Tyr | Gln | Glu | Leu | Thr | Arg | Leu | |
| | | | | 125 | | | | | 130 | | | | | 135 | | | |
| | | | | | | | | CCA | | | | | • | | | | 483 |
| | Lys | Ala | | Val | Gly | Glu | Leu | Pro | Glu | Lys | Ser | Lys | Leu | Gln | Glu | Ile | |
| 30 | | | 140 | | | | | 145 | | | | | 150 | | | | |
| | | | | | | | | AAG | | | | | | | | | 531 |
| | Tyr | | Glu | Leu | Thr | Arg | Leu | Lys | Ala | Ala | Val | G1y | Glu | Leu | Pro | Glu | |
| | | 155 | | | | | 160 | | | | | 165 | | | | | |
| | | | | | | | | TAC | | | | | | | | | 579 |
| 35 | | Ser | Lys | Leu | Gln | | Ile | Tyr | Gln | Glu | | Thr | Glu | Leu | Lys | | |
| | 170 | | ••- | | | 175 | | | | | 180 | | | | | 185 | |
| • | | | | | | | | AAA | | | | | | | | | 627 |
| | Ala | Val | Glv | Glu | Leu | Pro | Glu | Lvs | Ser | Lvs | Leu | Gln | Glu | Ile | Tvr | Gln | |

| | | | | | 190 | | | | | 195 | | | | | 200 | | |
|----|------|-------|------|-------|------|------|------|------|------|------|-----|------|-------|------|-------|-------|------|
| | GAG | CTG | ACC | CAG | CTG | AAG | GCT | GCA | GTG | GGT | GAG | TTG | CCA | GAC | CAG | TCC | 67. |
| | Glu | Leu | Thr | Gln | Leu | Lys | Ala | Ala | Val | Gly | Glu | Leu | Pro | Asp | Gln | Ser | |
| | | | | 205 | | | | | 210 | | | | • | 215 | | | |
| 5 | AAG | CAG | CAG | CAA | ATC | TAT | CAA | GAA | CTG | ACC | GAT | TTG | AAG | ACT | GĊA | TTT | 72 |
| | Lys | Gln | Gln | Gln | Ile | Tyr | Gln | Glu | Leu | Thr | Asp | Leu | Lys | Thr | Ala | Phe | |
| | | | 220 | | | | | 225 | | | | | 230 | | | | |
| | GAA | CGC | CTG | TGC | CGC | CAC | TGT | CCC | AAG | GAC | TGG | ACA | TTC | TTC | CAA | GGA | 771 |
| | Glu | Arg | Leu | Cys | Arg | His | Cys | Pro | Lys | Asp | Trp | Thr | Phe | Phe | Gln | Gly | |
| 10 | | 2,35 | | | | | 240 | | | | | 245 | | | | | |
| | AAC | TGT | TAC | TTC | ATG | TCT | AAC | TCC | CAG | CGG | AAC | TGG | CAC | GAC | TCC | GTC | 819 |
| | Asn | Cys | Tyr | Phe | Met | Ser | Asn | Ser | Gln | Arg | Asn | Trp | His | Asp | Ser | Val | |
| | 250 | | | | | 255 | | | | | 260 | | | | | 265 | |
| | ACC | GCC | TGC | CAG | GAA | GTG | AGG | GCC | CAG | CTC | GTC | GTA | ATC | AAA | ACT | GCT | 867 |
| 15 | Thr | Ala | Cys | Gln | Glu | Val | Arg | Ala | Gln | Leu | Val | Val | Ile | Lys | Thr | Ala | |
| | | | | | 270 | | | | | 275 | | | | | 280 | | |
| | GAG | GAG | CAG | CTT | CCA | GCG | GTA | CTG | GAA | CAG | TGG | AGA | ACC | CAA | CAA | | 912 |
| | Glu | Glu | Gln | Leu | Pro | Ala | Val | Leu | Glu | G1n | Trp | Arg | Thr | Gln | Gln | | |
| | | | | 285 | | | | | 290 | | | | | 295 | | | |
| 20 | TAGO | CGGGA | AT G | SAAGA | CTGT | G CG | GAAT | TTAG | TGG | CAGI | GGC | TGGA | ACGA | CA A | TCGA | TGT | 970 |
| | GACG | TTGA | CA A | ATTAC | TGGA | T CT | GCAA | AAAG | -ccc | GCAG | CCT | GCTT | CAGA | GA C | GAAT | AGTTG | 1030 |
| | TTTC | CCTG | CT A | GCCT | CAGC | C TC | CATT | GTGG | TAT | AGCA | GAA | CTTC | ACCC | AC I | TGTA | AGCCA | 1090 |
| | GCGC | CTTCT | TC T | CTCC | ATCC | T TG | GACC | TTCA | CAA | ATGC | CCT | GAGA | .CGGT | TC I | CTGT | TCGAT | 1150 |
| | TTTI | CATC | cc c | TATG | AACC | T GG | GTCT | TATT | CTG | TCCT | TCT | GATG | CCTC | CA A | GTTT. | CCCTG | 1210 |
| 25 | GTGT | AGAG | CT T | GTGT | TCTT | G GC | CCAT | CCTT | GGA | GCTT | TAT | AAGT | GACC | TG A | GTGG | GATGC | 1270 |
| | ATTI | 'AGGG | GG C | GGGC | TTGG | T AT | GTTG | TATG | AAT | CCAC | TCT | CTGT | TCCT | TT T | GGAG. | ATTAG | 1330 |
| | ACTA | TTTG | GA T | 'ȚCAT | GTGT | A GC | TGCC | CTGT | CCC | CTGG | GGC | TTTA | TCTC | AT C | CATG | CAAAC | 1390 |
| | TACC | ATCT | GC T | CAAC | TTCC | A GC | TACA | cccc | GTG | CACC | CTT | TTGA | CTGG | GG A | CTTG | CTGGT | 1450 |
| | TGAA | GGAG | CT C | ATCT | TGCA | G GC | TGGA | AGCA | CCA | GGGA | ATT | AATT | cccc | CA G | TCAA | CCAAT | 1510 |
| 30 | GGCA | TCCA | GA G | AGGG | CATG | G AG | GCTC | CATA | CAA | CCTC | TTC | CACC | CCCA | CA T | CTTT | CTTTG | 1570 |
| | TCCT | ATAC. | AT G | TCTT | CCAT | T TG | GCTG | TTTC | TGA | GTTG | TAG | CCTT | TATA | AT A | AAGT | GGTAA | 1630 |
| | ATGT | TGTA | AC T | GC | | | | | | | | | | | | | 1643 |

35 (2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 729
 - (B) TYPE: Nucleic acid

| | | | | (0) | OI. | MIDE | נים וועי | J . L | JOUDI | . e | | | | | | | |
|-----|-------|------|-------|-------|------|-------|-------------|-------|-------|-----------|-----------|------|------|------|-----------|-------|-----|
| | | | | (D) | TOP | OLOG | Y: L | inea | r | | | | | | | | |
| | | (| ii) | SEQU | ENCE | KIN | D: c | DNA | to m | RNA | • | | | | | | |
| 5 | | (| vi) | ORIG | INAL | . sou | RCE: | | | | | | | | | | |
| | | | | (A) | ORG | ANIS | M: <i>H</i> | ото | sapi | ens | | | | | | | |
| | | | | (B) | CEL | L KI | ND: | Ston | ach | cano | er | | | | | | |
| | | | | (D) | CLO | NE N | AME: | HPO | 1440 | ı | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| 10 | • | (| ix) | SEQU | ENCE | СНА | RACT | ERIS | TICS | : | | | | | | | |
| | | | | (A) | CHA | RACT | ERIZ | ATIO | N CO | DE: | CDS | | | | | | |
| | | | * : | (B) | EXI | STEN | CE P | OSIT | ION: | 38. | . 63 | 1 | | | | | |
| | | | | (C) | CHA | RACT | ERIZ | ATIO | n me | THOD | : E | | | | | | |
| | | | | | | | | | | | | | | | | | |
| 15 | | (| xi) | SEQU | ENCE | DES | CRIP | TION | : SE | Q ID | NO: | 40: | | | | | |
| | | | | | | | | | | | | | | | | | |
| | ACT' | TTCA | CTC . | ACCG | CCTG | TC C | TTCC | TGAC | A CC | TCAC | C AT | G TG | T AC | G GG | A AA | A TGT | 55 |
| | | | | | | | | | | | Me | t Cy | s Th | r Gl | y Ly | s Cys | |
| | | | | | | | | | | | | 1 | | | | 5 | |
| 20 | | | | | | | | | | | | | | | TGC | | 103 |
| ٠ | Ala | Arg | Cys | Val | Gly | Leu | Ser | Leu | Ile | Thr | Leu | Cys | Leu | Val | Cys | Ile | |
| | | | | 10 | | | | | 15 | | | | | 20 | | | |
| | | | | | | | | | | | | | | | TGG | | 151 |
| | Val | Ala | | | Leu | Leu | Leu | Val | Pro | Asn | Gly | Glu | Thr | Ser | Trp | Thr | |
| 25 | | | 25 | | | | | 30 | | | | | 35 | | | | |
| | | | | | | | | | | | | | | | TTC | | 199 |
| | Asn | | Asn | His | Leu | Ser | | Gln | Val | Trp | Leu | | Gly | Gly | Phe | Ile | |
| | 000 | 40 | 000 | 0.004 | 4.50 | 0.50 | 45 | | | | | 50 | | | | | |
| 30 | | | | | | | | | | | | | | | CGG | | 247 |
| , , | 55 | GIY | Gry | Leu | Mec | 60 | Leu | Cys | Pro | GIÀ | | ATA | AIA | Val | Arg | | |
| | | GGC | AAC | ccc | TCC | | CCT | CCT | 000 | mcc. | 65 mcm | CC 4 | 440 | ccc | WCC. | 70 | 205 |
| | | | | | | | | | | | | | | | TGC | | 295 |
| | O L y | ory | шуз | Gry | 75 | cys | Gly | MIS | Gly | | Cys | GIA | ASI | Arg | Cys | Arg | |
| 35 | ATG | CTG | CGC | TCG | | TTC | TCC | ፐርር | GCG | 80 TTC | GGG | GTG | ርሞጥ | сст | 85 GCC | ATC: | 343 |
| | | | | | | | | | | | | | | | Ala | | 373 |
| | | | | 90 | | | | ~~* | 95 | | , | | Dou | 100 | | | |
| | TAC | TGC | СТС | | GTG | ፐርጥ | GGA | GCT | | CTC | CGA | ጥልል | GG A | | AGA | TGC | 391 |

| | Tyr | Cys | Leu | Ser | Val | Ser | Gly | Ala | Gly | Leu | Arg | Asn | Gly | Pro | Arg | Cys | * |
|-----|------|------|-------|------|-----------|-------|-------|-------|-------------|------|-----|------|------|------|------|--------|-----|
| | | | 105 | | | | | 110 | | | | | 115 | | | | |
| | TTA | ATG | AAC | GGC | GAG | TGG | GGC | TAC | CAC | TTC | GAA | GAC | ACC | GCG | GGA | GCT | 439 |
| | Leu | Met | Asn | Gly | Glu | Trp | Gly | Tyr | His | Phe | Glu | Asp | Thr | Ala | Gly | Ala | |
| 5 | | 120 | | | | | 125 | | | | | 130 | | | | | |
| | TAC | TTG | CTC | AAC | CGC | ACT | CTA | TGG | GAT | CGG | TGC | GAG | GCG | ccc | CCT | CGC | 487 |
| | Tyr | Leu | Leu | Asn | Arg | Thr | Leu | Trp | Asp | Arg | Сув | Glu | A1a | Pro | Pro | Arg | |
| | 135 | | | | | 140 | | | | | 145 | | | | | 150 | |
| | GTG | GTC | CCC | TGG | AAT | GTG | ACG | CTC | TTC | TCG | CTG | CTG | GTG | GCC | GCC | TCC | 535 |
| 10 | Val | Val | Pro | Trp | Asn | Val | Thr | Leu | Phe | Ser | Leu | Leu | Val | Ala | Ala | Ser | |
| | | | | | 155 | | | | | 160 | | | | | 165 | | |
| | TGC | CTG | GAG | ATA | GTA | CTG | TGT | GGG | ATC | CAG | CTG | GTG | AAC | GCG | ACC | ATT | 583 |
| | Cys | Leu | G1u | Ile | Val | Leu | Cys | Gly | Ile | Gln | Leu | Val | Asn | Ala | Thr | Ile | |
| | | | , | 170 | | | | | 175 | | | | | 180 | | | |
| 15 | GGT | GTC | TTC | TGC | GGC | GAT | TGC | AGG | AAA | AAA | CAG | GAC | ACC | CCT | CAC | TG | 630 |
| | Gly | Val | Phe | Cys | Gly | Asp | Cys | Arg | Lys | Lys | Gln | Asp | Thr | Pro | His | | |
| | | | 185 | | | | | 190 | | | | | 195 | | | | |
| | AGG | TCCA | ACT (| ACC | CCG | G TI | ACAC | CTGC | TCC | TTCC | TGG | ACGC | CTAC | CT G | GCTC | CGCTCA | 690 |
| | CTCC | CTT | CT C | GCTA | AGAAT | CA AA | CTGC | TTTG | CGC | TCTC | TT | | | | | | 729 |
| 20 | | | | | | | | | | | | | | | | • | |
| | | | | | | | | | | | | | | | | | |
| | (2) | | | | | SEQ | | | | | | | | | | | |
| | | (1 | .) SE | | | HARA | | | CS: | | | | | | | | |
| 2 5 | | | | | | TH: | | | | | | | | | | | |
| 25 | ٠. | | | | | : Nu | | | | | | | | | | | |
| | | | | | | NDED | | | | | | | | | | | |
| | | , : | ٠. ٥ | | | LOGY | | | | ••• | | | | | | | |
| | | (1 | .1) 5 | EQUE | ENCE | KIND | i: CD | NA t | o mk | NA | | | | | | | |
| 30 | | (17 | .i. 0 | ртст | ' N 7 A 7 | SOUR | CF. | | • | | | | | | | | |
| | | (• | 1, 0 | | | NISM | | .mo c | ania | 20 | | | | | | | |
| | | | | | | KIN | | | • | | | | | | | | |
| | | | | | | E NA | | | | ance | L | | | | | | |
| | | | | ()) | CLON | E NA | rib: | ULOI | J Z0 | | | | | | | | |
| 35 | | (i | x) S | EQUE | NCE | CHAR | ACTE | RIST | ics: | | | | | | | | |
| | | | | - | | ACTE | | | | E: C | DS | | | | | | |
| | | | | | | TENC | | | | | | | | | | | |
| | | | | | | ACTE | | | | | | | | | | | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

| | GAG | CCGC. | AGG | TCTG | GGCT | GC A | GTAG | GTCC | C GG | CAA | CCGC. | A GG | CTCG | CGGC | GGG | CGC | TGGG | 6 | 0 |
|-----|-------|-------|-----|------|-------------|------|------|-------|------|-------|-------|-------|-------|-------|------------|-----------|------|------|---|
| | CGC | GGGA | TCC | GACT | CTAG | TC G | TA A | TG G | AG G | CG (| GGC · | GGC | TTT | CTG | GAC | TCG | CTC | 11 | 3 |
| 5 | | | | | | | М | et G | lu A | la (| 31y | Gly | Phe | Leu | Asp | Ser | Leu | | |
| | | | | | | | | 1 | | | | . 5 | | | | | 10 | | |
| | ATT | TAC | GGA | GCA | TGC | GTG | GTC | TTC | ACC | CT | r GG | C AT | G TT | с тс | C GC | C G | 3C | 16 | 1 |
| | Ile | Tyr | Gly | Ala | Ċys | Val | Val | Phe | Thr | Let | ı G1 | у Ме | t Ph | e Se | r Al | a G | ly | | |
| | | | | | 15 | | | | | 20 |) | | | | 2 | 5 | | | |
| 10 | CTC | TCG | GAC | CTC | AGG | CAC | ATG | CGA | ATG | ACC | CGG | G AG | T GT | G GA | C AA | C G | rc | 209 | 9 |
| | Leu | Ser | Asp | Leu | Arg | His | Met | Arg | Met | Thi | . Ar | g Se | r Va | l As | p As | n Ve | al | | |
| | | | | 30 | | | | | 35 | | | | | 4 | 0 | | | | |
| | CAG | TTC | CTG | CCC | TTT | CTC | ACC | ACG | GAA | GTO | AA C | C AA | C CT | G GG | C TG | 3 C: | ľG | 257 | 7 |
| | G1n | Phe | Leu | Pro | Phe | Leu | Thr | Thr | Glu | Va] | l Ası | n Ası | n Le | u G1 | y Tr | p Le | eu | | |
| 15 | | | 45 | | | | | 50 | | | | | 5 | 5 | | | | | |
| | AGT | TAT | GGG | GCT | TTG | AAG | GGA | GAC | GGG | ATO | CTO | CAT | C GT | C GT | C AA | CAC | CA | 305 | 5 |
| | Ser | Tyr | Gly | Ala | Leu | Lys | Gly | Asp | Gly | Ile | Lei | ı Il | e Vai | l Va | l Ası | n Th | ır | | |
| | | 60 | | | | | 65 | | | | | 70 | 0 | | | | | | |
| | GTG | GGT | GCT | GCG | CTT | CAG | ACC | CTG | TAT | ATC | TTO | G GC | A TA | r ct(| G CA | T.A | C | 353 | 3 |
| 20 | Val | G1y | Ala | Ala | Leu | Gln | Thr | Leu | Tyr | Il€ | Lei | ı Ala | а Ту | r Lei | u Hi | з Ту | r | | |
| | 75 | | | • | | 80 | | | | | 8. | 5 | | • | | ç | 0 | | |
| | TGC | CCT | CGG | AAG | CGT | GTT | GTG | CTC | CTA | CAG | ACT | GC/ | A AC | CTC | G CTA | A GG | G | 401 | Ĺ |
| | Cys | Pro | Arg | Lys | Arg | Val | Val | Leu | Leu | Gln | Thi | : A1 | a Thi | r Lei | ı Lev | 1 G1 | .у | | |
| | | | | | 95 | | | | | 100 | | | | | 105 | | | | |
| 25 | | | | | | | | | | | | | | | C AAC | | | 449 | , |
| | Val | Leu | Leu | | Gly | Tyr | Gly | Tyr | | Trp | Lei | ı Lei | ı Val | | Asr | ı Pr | .0 | | |
| | | | | 110 | | | | | 115 | | | | | 120 | | | | | _ |
| | | | | | | | | | | | | | | | C ACC | | | 497 | , |
| 20 | Glu | AIA | | Leu | Gln | Gln | Leu | - | Leu | Phe | Cys | Ser | | | Thr | : 11 | e | | |
| 30 | 400 | 4.00 | 125 | 0.00 | 50 4 | | | 130 | | | | | 135 | | | | | | |
| | | | | | | | • | | | | | | | | CAA | | | 545 | , |
| | ser | | Tyr | Leu | Ser | Pro | | Ala | Asp | Leu | Ala | | | . 116 | e Glr | Th | r | | |
| | | 140 | 400 | | mom | 0.00 | 145 | | | | | 150 | | | | | | 500 | |
| 2 5 | | | | | | | | | | | | | | | CTI | | | 593 | • |
| 35 | | ser | inr | GIN | cys | | ser | Tyr | Pro | reu | | | : Ala | Thr | Leu | | | | |
| | 155 | ጥርጥ | ccc | ሞርር | ሞርር | 160 | СТС | m a m | ccc | m m m | 165 | | | | | 17 • • | | 61.1 | |
| | | | | | | | | | | | | | | | CCC Pro | | | 641 | |
| | T 11T | SET | UTG | OCI | Trh | Uy S | ueu | T À L | υLΆ | rue | - AID | Let | T WIE | , ASI | , r.c | , ⊥y | 4 | | |

| | 175 180 185 | |
|-----|---|------|
| | ATC ATG GTG TCC AAC TTT CCA GGA ATC GTC ACC AGC TTT ATC CGC TTC | 689 |
| | Ile Met Val Ser Asn Phe Pro Gly Ile Val Thr Ser Phe Ile Arg Phe | 009 |
| | 190 195 200 | |
| 5 | TGG CTT TTC TGG AAG TAC CCC CAG GAG CAA GAC AGG AAC TAC TGG CTC | 737 |
| | Trp Leu Phe Trp Lys Tyr Pro Gln Glu Gln Asp Arg Asn Tyr Trp Leu | ,,, |
| | 205 210 215 | |
| | CTG CAA ACC TGAGGCTGCT CATCTGACCA CTGGGCACCT TAGTGCCAAC CTGA | 790 |
| | Leu Gln Thr | |
| 10 | 220 | |
| | ACCAAAGAGA CCTCCTTGTT TCAGCTGGGC CTGCTGTCCA GCTTCCCAGG TGCAGTGGGT | 850 |
| | TGTGGGAACA AGAGATGACT TTGAGGATAA AAGGACCAAA GAAAAAGCTT TACTTAGATG | 910 |
| | ATTGATTGGG GCCTAGGAGA TGAAATCACT TTTTATTTTT TAGAGATTTT TTTTTTTAAT | 970 |
| | TTTGGAGGTT GGGGTGCAAT CTTTAGAATA TGCCTTAAAA GGCCGGGCGC GGTGGCTCAC | 1030 |
| 15 | GCCTGTAATC CCAGCACTTT GGGAGGCCAA GGTGGGCGGA TCGCCTGAGG TCAGGAGTTC | 1090 |
| | AAGACCAACC TGACTAACAT GGTGAAACCC CATCTCTACT AAAAATACAA AATTAGCCAG | 1150 |
| | GCATGATGGC ACATGCCTGT AATCCCAGAT ACTTGGGAGG CTGAGGCAGG AGAATTGCTT | 1210 |
| | GAACCCAGGA GGTGGAGGTT GCAGTGAGCT GAGATCGTGC CATTGTGATA TGAATATGCC | 1270 |
| | TTATATGCTG ATATGAATAT GCCTTAAAAT AAAGTGTTCC CCACCCCTGC CC | 1322 |
| 20 | | |
| | | |
| | (2) INFORMATION FOR SEQ ID NO: 42: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| 0.5 | (A) LENGTH: 3045 | |
| 25 | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| 30 | (wi) OBIGINAL COMOR | |
| 30 | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer | |
| | (D) CLONE NAME: HP10230 | |
| | (D) ODOUT WELD: HEIOSON | |
| 35 | (ix) SEQUENCE CHARACTERISTICS: | |
| | (A) CHARACTERIZATION CODE: CDS | |
| | (B) EXISTENCE POSITION: 191 946 | |
| | (C) CHARACTERIZATION METHOD: E | |

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

| | GTT | TCGC | CTC | AGAA | GGCI | GC C | TCGC | TGGI | C .CC | TAA | CGGT | r GGC | GCCA | CGT | CCG | CCCGTCT | . 6 | (|
|------|-------------|--------------|-------|------|------|-------------|-------|------|-------|-------|------|-------------|-------|------------|-------|---------|------|----|
| | CCG | CCTT | CTG | CATC | GCGG | CT I | CGGC | GGCI | T CC | CACCI | AGAC | ACC | CTAAC | AGT | CGC | GAGCCG | 12 | |
| 5 | GCC | GCGT | CGT | GAGG | GGGT | CG G | CACG | GGGA | G TO | GGGC | GGTC | TTG | TGCA | TCT | TGG | CTACCTG | 180 | |
| | TGG | GTCG | AAG . | ATG | TCG | GAC | ATC | GGA | GAC | TGG | TTC | AGG | AGC | ATC | CCG | GCG | 229 | ç |
| | | | 1 | Met | Ser | Asp | Ile | Gly | Asp | Trp | Phe | Arg | Ser | Ile | Pro | Ala | | |
| | | | | 1 | | | | 5 | | | | | 10 | | | | | |
| | ATC | ACG | CGC | TAT | TGG | TTC | GCC | GCC | ACC | GTC | GCC | GTG | ccc | TTG | GTO | GGC | 27 | 7 |
| 10 | Ile | Thr | Arg | Tyr | Trp | Phe | Ala | Ala | Thr | Val | Ala | Val | Pro | Leu | Val | . Gly | | |
| | | 15 | | | | | 20 | | | | | 25 | ; | | | | | |
| | AAA | CTC | GGC | CTC | ATC | AGC | CCG | GCC | TAC | CTC | TTC | CTC | TGG | ccc | GAA | GCC | 325 | ĵ |
| | Lys | Leu | Gly | Leu | Ile | Ser | Pro | Ala | Tyr | Leu | Phe | Leu | Trp | Pro | G1u | Ala | | |
| | 30 | | | | | 35 | | | | | 40 |) | | | | 45 | | |
| 15 | TTC | CTT | TAT | CGC | TTT | CAG | ATT | TGG | AGG | CCA | ATC | ACT | GCC | ACC | TTT | TAT | 373 | \$ |
| | Phe | Leu | Tyr | Arg | Phe | Gln | Ile | Trp | Arg | Pro | Ile | Thr | Ala | Thr | Phe | Tyr | | |
| | | | | | 50 | | | | | 55 | ı | | | | 60 | | | |
| | TTC | CCT | GTG. | GGT | CCA | GGA | ACT | GGA | TTT | CTT | TAT | TTG | GTC | AAT | TTA | TAT | 421 | - |
| | Phe | Pro | Val | Gly | Pro | Gly | Thr | Gly | Phe | Leu | Tyr | Leu | Val | Asn | Leu | Tyr | | |
| 20 | • | | | 65 | | | | | 70 | | | | | 75 | | | | |
| | | | | | | | | | | | | | | TTT | | | 469 |) |
| | Phe | Leu | | Gln | Tyr | Ser | Thr | _ | | Glu | Thr | Gly | | Phe | Asp | Gly | | |
| | | | 80 | | | | | 85 | | | | | 90 | | | | | |
| 0.5 | | | | | | | | | | | | | | ATT | | | 517 | |
| 25 | Arg | | Ala | Asp | Tyr | Leu | | Met | Leu | Leu | Phe | | - | Ile | Cys | Ile | | |
| | | 95 | | | | | 100 | | | | | 105 | | | | | | |
| | | | | | | | | * | | | | | | ATT | | | 565 | |
| | | IIe | Thr | GIŻ | ren | | | Asp | Met | Gin | | | Met | Ile | Pro | | | |
| 3 () | 110 | A TP.C | TC A | CTA | CTT | 115 | | mcc. | 666 | 040 | 120 | | 404 | CAC | A TOC | 125 | 612 | |
| 30 | | | | | | | | | | | | | | GAC | | | 613 | |
| | 116 | Mer | ser | var | | - | Val | irp | AIB | | | Asn | Arg | Asp | | | | |
| | CTA. | ም ር ለ | ատա | TCC | 130 | | A C A | CCA | ጥጥጥ | 135 | | ሞርር | ጥለጥ | ጥጥል | 140 | | 661 | |
| | | | | | | | | | | | | | | TTA | | | 661 | |
| 35 | Val | Ser | rne | 145 | rne | GIY | 1111 | ALE | | • | Ala | Cys | ıyı | Leu | FIO | ırþ | | |
| | G ምሞ | ATC | Стт | | ጥጥሮ | AA C | ጥ∆ጥ | Δጥር | 150 | | GGC | ጥ ርር | ርጥል | 155 ATC | ልልጥ | GAG | 709 | |
| | | | | | | | | | | | | | | Ile | | | , 09 | |
| | | | 160 | 013 | | 41011 | - , . | 165 | TTC | GIY | GIY | 967 | 170 | 116 | 44011 | 514 | | |
| | | | | | | | | 200 | | | | | -,0 | | | | | |

| | CTT ATT GG | A AAT CTG | GTT GGA CAT | CTT TAT TTT | TTC CTA ATG | TTC AGA | 757 |
|------|-------------|-------------|--|----------------|---------------------|------------------|------|
| | Leu Ile Gl | y Asn Leu ' | Val Gly His | Leu Tyr Phe | Phe Leu Met | Phe Arg | |
| | 175 | | 180 | | 185 | | |
| | TAC CCA AT | G GAC TTG | GGA GGA AGA | AAT TTT CTA | TCC ACA CCT | CAG TTT | 805 |
| 5 | Tyr Pro Me | t Asp Leu (| Gly Gly Arg | Asn Phe Leu | Ser Thr Pro | Gln Phe | |
| | 190 | 2 | 195 | 200 | | 205 | |
| • | TTG TAC CG | C TGG CTG (| CCC AGT AGG | AGA GGA GGA | GTA TCA GGA | TTT GGT | 853 |
| | Leu Tyr Ar | g Trp Leu I | Pro Ser Arg | Arg Gly Gly | Val Ser Gly | Phe Gly | |
| | | 210 | | 215 | | 220 | |
| 10 | GTG CCC CC | T GCT AGC A | ATG AGG CGA | GCT GCT GAT | CAG AAT GGC | GGA GGC | 901 |
| | Val Pro Pro | o Ala Ser N | fet Arg Arg | Ala Ala Asp | Gln Asn Gly | Gly Gly | |
| | | 225 | | 230 | 235 | | |
| | GGG AGA CAG | C AAC TGG G | GC CAG GGC | TTT CGA CTT | GGA GAC CAG | TGAAGGG | 950 |
| | Gly Arg His | s Asn Trp G | Sly Gln Gly | Phe Arg Leu | Gly Asp Gln | | |
| 15 | 240 | 0 | 245 | | 250 | | |
| | GCGGCCTCGG | GCAGCCGCTC | CTCTCAAGCC | ACATTTCCTC | CCAGTGCTGG | GTGCGCTTAA | 1010 |
| | CAACTGCGTT | CTGGCTAACA | CTGTTGGACC | TGACCCACAC | TGAATGTAGT | CTTTCAGTAC | 1070 |
| | | | | ATATAAGTGT | | | 1130 |
| | CATTCAAGTC | CTTACTGCTG | TGAAGAACAA | ATACCAACTG | TGCAAATTGC | AAAACTGACT | 1190 |
| 20 | ACATTTTTG | GTGTCTTCTC | TTCTCCCCTT | TCCGTCTGAA | TAATGGGTTT | PAGCGGGTCC | 1250 |
| | TAGTCTGCTG | GCATTGAGCT | GGGGCTGGGT | CACCAAACCC | TTCCCAAAAG (| GACCCTTATC | 1310 |
| | | | | TTTCCCAACC | | | 1370 |
| | | | • | CAGGTTCTGT | | | 1430 |
| | | | | TTTTCCCCCT | | | 1490 |
| 25 . | | | | CGTTTTCTCA | | | 1550 |
| | | | | TTCAGATATT | | | 1610 |
| | | | | GAGATACGAG | • | | 1670 |
| | | | | GAGTTGCAGC | | / . | 1730 |
| 2.0 | | | | TATGTAGGCC | | | 1790 |
| 30 | | | | CCAGATCATG | • | | 1850 |
| | | | | TTTCAATCTC | | | 1910 |
| | | | | TTTAAATGTC . | | | 1970 |
| | | | | GAAGGCGCAG | | | 2030 |
|) E | | | | GGGAATAACA | | | 2090 |
| 35 | | | | ATTTTGAGTC | | • | 2150 |
| | | | | TTTTCGTAGG | | | 2210 |
| | | | | GGCCATGGCT | | TATTTTATT | 2270 |
| | A PATGACGTT | | $\Delta C \Delta C T C T T T \Delta C$ | - ሮአሮሮአሮሞአጥጥ / | 2804000 0 40 | αι ας ηνηνηνής Δ | 322N |

133

| | | ĢGCAACTAAA | AAGGCTTCAA | ACGTTTTGAT | CAGTTTCTTT | TCAGGAAACA | TTGTGCTCTA | 2390 |
|-----|---|------------|------------|------------|------------|------------|------------|------|
| | | ACAGTATGAC | TATTCTTTCC | CCCACTCTTA | AACAGTGTGA | TGTGTGTTAT | CCTAGGAAAT | 2450 |
| | | GAGAGTTGGC | AAACAACTTC | TCATTTTGAA | TAGAGTTTGT | GTGTACCTCT | CCATATTTAA | 2510 |
| | | TTTATATGAT | AAAATAGGTG | GGGAGAGTCT | GAACCTTAAC | TGTCATGTTT | TGTTGTTCAT | 2570 |
| | 5 | CTGTGGCCAC | AATAAAGTTT | ACTTGTAAAA | TTTTAGAGGC | CATTACTCCA | ATTATGTTGC | 2630 |
| | | ACGTACACTC | ATTGTACAGG | CGTGGAGACT | CATTGTATGT | ATAAGAATAT | TCTGACAGTG | 2690 |
| | | AGTGACCCGG | AGTCTCTGGT | GTACCCTCTT | ACCAGTCAGC | TGCCTGCGAG | CAGTCATTTT | 2750 |
| | | TTCCTAAAGG | TTTACAAGTA | TTTAGAACTC | TTCAGTTCAG | GGCAAAATGT | TCATGAAGTT | 2810 |
| | | ATTCCTCTTA | AACATGGTTA | GGAAGCTGAT | GACGTTATTG | ATTTTGTCTG | GATTATGTTT | 2870 |
| · 1 | 0 | CTGGAATAAT | TTTACCAAAA | CAAGCTATTT | GAGTTTTGAC | TTGACAAGGC | AAAACATGAC | 2930 |
| | | AGTGGATTCT | CTTTACAAAT | TGAAAAAAA | AATCCTTATT | TTGTATAAAG | GACTTCCCTT | 2990 |
| : | | TTTGTAAACT | AATCCTTTTT | ATTGGTAAAA | ATTGTAAATT | AAAATGTGCA | ACTTG | 3045 |
| | | | | | | | | |

- 15 (2) INFORMATION FOR SEQ ID NO: 43:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 653
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 20 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Epidermoid carcinoma
 - (C) CELL LINE: KB
 - (D) CLONE NAME: HP10389
 - (ix) SEQUENCE CHARACTERISTICS:
- 30 (A) CHARACTERIZATION CODE: CDS

35

- (B) EXISTENCE POSITION: 63.. 383
- (C) CHARACTERIZATION METHOD: E
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

ATGACCTTCA CCGGGAGGCT GAGGTCGGAG TCCCGATTTT CTCCTGCTGC TGTGGCCCGG

AC ATG GCG ACT CCC GGC CCT GTG ATT CCG GAG GTC CCC TTT GAA CCA

Met Ala Thr Pro Gly Pro Val Ile Pro Glu Val Pro Phe Glu Pro

134

| | | 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
|----|------|------|-------|------|------|---|-------|------|-------|------|-----|--------|---|-------|-------|----------------|------------|--|
| | TCG | AAG | CCT | CCA | GTC | ATT | GAG | GGG | CTG | AGC | CCC | ACT | GTT | TAC | AGG | AAT | 155 | |
| | Ser | Lys | Pro | Pro | Val | Ile | Glu | Gly | Leu | Ser | Pro | Thr | Val | Tyr | Arg | Asn | | |
| | | | | | 20 | | | | | 25 | | | | | 30 | | | |
| 5 | CCA | GAG | AGT | TTC | AAG | GAA | AAG | TTC | GTT | CGC | AAG | ACC | CGC | GAG | AAC | CCG | 203 | |
| | Pro | Glu | Ser | Phe | Lys | Glu | Lys | Phe | Val | Arg | Lys | Thr | Arg | Glu | Asn | Pro | | |
| | | | | 35 | | | | | 40 | | | | | 45 | | | | |
| | GTG | GTA | CCC | ATA | GGT | TGC | CTG | GCC | ACG | GCG | GCC | GCC | CTC | ACC | TAC | GGC | 251 | |
| | Val | Val | Pro | Ile | Gly | Cys | Leu | Ala | Thr | Ala | Ala | Ala | Leu | Thr | Tyr | Gly | | |
| 10 | | | 50 | | | | | 55 | | | | | 60 | | | | | |
| | | | | | | | | | | | | | | | ATG | | 299 | |
| • | Leu | Tyr | Ser | Phe | His | Arg | Gly | Asn | Ser | Gln | Arg | Ser | Gln | Leu | Met | Met | | |
| | | 65 | | | | | 70 | | | | | 75 | | | | | | |
| | | | | | | | | | | | | | | | TTG | | 347 | |
| 15 | Arg | Thr | Arg | Ile | Ala | | Gln | G1y | Phe | Thr | Val | Ala | Ala | Ile | Leu | Leu | | |
| | 80 | | | | | 85 | | | | | 90 | | | | | 95 | | |
| | | | | | | | | | | | | TAAG | CCCA | AGG (| STCTO | GCCTT | 400 | |
| | Gly | Leu | Ala | Val | | Ala | Met | Lys | Ser | • | Pro | | | | | | | |
| 20 | | 0000 | 200 0 | | 100 | | | 4000 | | 105 | | 0.40 | | | | 100010 | 4.60 | |
| 20 | | | | | | | | | | | | | | | | GGGAC TTGTG | | |
| | | | | | | | | | | | | | | | | CATACT | 520 580 | |
| | | | | | | | | | | | | | | | | ACTTG | 640 | |
| | TATT | | | | | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | 1001 | | , 001 | | | 111110 | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | | | | 653 | |
| 25 | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | (2) | INFO | RMAI | ION | FOR | SEQ | ID N | 0: 4 | 4: | | | | | | | | | |
| | | (i |) SE | QUEN | CE C | HARA | .CTER | ISTI | :cs | | | | | | | | | |
| | | | | (A) | LENG | TH: | 439 | | | | | | | | | | | |
| 30 | | | | (B) | TYPE | : Nu | clei | c ac | id | | | | | | | | | |
| | | | | (C) | STRA | NDED | NESS | : Do | uble | ! | | | | | | | | |
| | | | | (D) | TOPO | LOGY | : Li | near | • | | | | | | | | | |
| | | (i | i) S | EQUE | NCE | KIND | : cD | NA t | o mR | NA | | | | | | | | |
| 35 | | (v | i) 0 | RIGI | NAL | SOUR | CE: | | | | | | | | | | | |
| | | | | (A) | ORGA | NISM | : Ho | mo s | apie | ns | | | | | | | | |
| | | | | (B) | CELL | KIN | D: S | toma | ch c | ance | r | | | | | | | |

(D) CLONE NAME: HP10408

135

(A) CHARACTERIZATION CODE: CDS

(ix) SEQUENCE CHARACTERISTICS:

| | | (B) EXI | STENCE P | OSITION: | 75, 31 | .1 | | |
|----|--------------|-----------|-----------|----------|----------|----------|-----------|-----------|
| | | (C) CHA | RACTERIZ. | ATION ME | THOD: E | | | |
| 5 | | 1 | | | | | | |
| | (xi) | SEQUENCE | DESCRIP | TION: SE | Q ID NO: | 44: | | |
| ٠ | GTAGAAACAG | GCCTGTTA | AG GAGAG | GCCAC CG | GGACTTCA | GTGTCTC | CTC CATC | CCAGGA 60 |
| | GCGCAGTGGC | CACT ATG | GGG TCT | GGG CTG | CCC CTT | GTC CTC | CTC TTG | ACC 110 |
| 10 | | Met | Gly Ser | Gly Leu | Pro Leu | Val Leu | Leu Leu | Thr |
| | | 1 | | 5 | | | 10 | |
| | CTC CTT GGC | AGC TCA | CAT GGA | ACA GGG | CCG GGT | ATG ACT | TTG CAA | CTG 158 |
| | Leu Leu Gly | Ser Ser | His Gly | Thr Gly | Pro Gly | Met Thr | Leu Gln | Leu |
| | 15 | | | 20 | | 25 | | |
| 15 | AAG CTG AAG | GAG TCT | TTT CTG | ACA AAT | TCC TCC | TAT GAG | TCC AGC | TTC 206 |
| | Lys Leu Lys | Glu Ser | Phe Leu | Thr Asn | Ser Ser | Tyr Glu | Ser Ser | Phe |
| | 30 | | 35 | | | 40 | | • |
| | CTG GAA TTG | CTT GAA | AAG CTC | TGC CTC | CTC CTC | CAT CTC | CCT TCA | GGG 254 |
| | Leu Glu Leu | Leu Glu | Lys Leu | Cys Leu | Leu Leu | His Leu | Pro Ser | Gly |
| 20 | 45 | | 50 | | 55 | | | 60 |
| | ACC AGC GTC | ACC CTC | CAC CAT | GCA AGA | TCT CAA | CAC CAT | GTT GTC | TGC 302 |
| | Thr Ser Val | Thr Leu | His His | Ala Arg | Ser Gln | His His | Val Val | Cys |
| | | 65 | | • | 70 | | 75 | |
| | AAC ACA TGAG | CAGCCAT 1 | GAAGCCTG | т стсстт | CTTG GC | CCGGGCTT | TTGGGCCG | GG GA 360 |
| 25 | Asn Thr | | | | | | | |
| | | | | | | | | |
| | TGCAGGAGGC A | AGGCCCCGA | C CCTGTC | TTTC AGO | AGGCCCC | CACCCTC | CTG AGTGG | CAATA 420 |
| | AATAAAATTC (| GGTATGCTG | ; | | | | | 439 |
| | | | | | | | | |
| 30 | | | | | | | | |
| | (2) INFORMAT | TION FOR | SEQ ID N | 10: 45: | | | | |
| | (i) SI | EQUENCE C | HARACTER | ISTICS: | | | | |
| | | (A) LENG | TH: 1131 | | | | • | |
| | | (B) TYPE | : Nuclei | c acid | | | | |
| 35 | | (C) STRA | NDEDNESS | : Double | | | | |
| | | (D) TOPO | LOGY: Li | near | | | | |
| | (ii) S | SEQUENCE | KIND: cD | NA to mR | NA | | | |

| | | (| vi) (| ORIG | INAL | sou | RCE: | | | | | | | | | | |
|----|-----|-------|-------|------|------|-------|-------|-------|-------|-------|------|-----|------|-------|------|------------------|-----|
| | | | | (A) | ORG | ANISI | 1: H | ото | sapi | ens | | | | | | | |
| | | | | (B) | CEL | L KI | ND: | Stom | ach (| canc | er | | | | | | |
| | | | | (D) | CLO | NE NA | AME: | HP1 | 0412 | | | | | | | | |
| 5 | | | | | | | | | | | | | | | | | |
| | | (: | ix) | SEQU | ENCE | CHAI | RACT | ERIS' | rics | : | | | | | | | |
| | | | | (A) | CHAI | RACTI | ERIZA | ATIO | N CO | DE: (| CDS | | | | | | |
| | | | | (B) | EXI | STEN | CE P | OSIT: | ION: | 56. | . 10 | 00 | • | | | | |
| | | | | (C) | CHAI | RACTI | ERIZA | ATIO | ME | THOD | : E | | | | | | |
| 10 | | | | | | | | | | | | | | | | | |
| | | (: | xi) : | SEQU | ENCE | DES | CRIP' | rion | : SEC | Q ID | NO: | 45: | | | | | |
| | CTA | rgag. | ATC (| CCGG | CCTC | AG GO | STGG | ACGC | A GT | GGTT | CTGC | ACT | GAGG | ccc ' | TCGT | C ATG | 58 |
| | | | | | | | | | | | | | | | | Met | |
| 15 | | | | | | | | | | | | | | | | 1 | |
| | GTG | GCG | CCT | GTG | TGG | TAC | TTG | GTA | GCG | GCG | GCT | CTG | CTA | GTC | GGC | TTT | 106 |
| | Val | Ala | Pro | Val | Trp | Tyr | Leu | Va1 | Ala | Ala | Ala | Leu | Leu | Val | Gly | Phe | |
| | | | | 5 | | | | | 10 | | | | | 15 | | | |
| | ATC | CTC | TTC | CTG | ACT | CGC | AGC | CGG | GGC | CGG | GCG | GCA | TCA | GCC | GGC | CAA | 154 |
| 20 | Ile | Leu | Phe | Leu | Thr | Arg | Ser | Arg | Gly | Arg | Ala | Ala | Ser | Ala | Gly | Gln | |
| | | | 20 | | | | | 25 | | | | | 30 | | | | |
| | GAG | CCA | CTG | CAC | AAT | GAG | GAG | CTG | GCA | GGA | GCA | GGC | CGG | GTG | GCC | CAG | 202 |
| | Glu | Pro | Leu | His | Asn | Glu | Glu | Leu | Ala | Gly | Ala | Gly | Arg | Val | Ala | Gln | |
| | | 35 | | | | | 40 | | | | | 45 | | | | | |
| 25 | CCT | GGG | CCC | CTG | GAG | CCT | GAG | GAG | CCG | AGA | GCT | GGA | GGC | AGG | CCT | CGG | 250 |
| | Pro | Gly | Pro | Leu | Glu | Pro | Glu | Glu | Pro | Arg | Ala | Gly | Gly | Arg | Pro | Arg | |
| | 50 | | | | | 55 | | | | | 60 | | | | | 65 | |
| | CGC | CGG | AGG | GAC | CTG | GGC | AGC | CGC | CTA | CAG | GCC | CAG | CGT | CGA | GCC | CAG | 298 |
| | Arg | Arg | Arg | Asp | Leu | Gly | Ser | Arg | Leu | Gln | Ala | Gln | Arg | Arg | Ala | Gln | |
| 30 | | | | | 70 | | | | | 75 | | | | | 80 | | |
| | CGG | GTG | GCC | TGG | GCA | GAA | GCA | GAT | GAG | AAC | GAG | GAG | GAA | GCT | GTC | ATC | 346 |
| | Arg | Va1 | Ala | Trp | Ala | Glu | Ala | Asp | Glu | Asn | Glu | Glu | Glu | Ala | Val | Ile | |
| | • | | | 85 | | | | | 90 | | | | | 95 | | | |
| | CTA | GCC | CAG | GAG | GAG | GAA | GGT | GTC | GAG | AAG | CCA | GCG | GAA | ACT | CAC | CTG | 394 |
| 35 | Leu | Ala | Gln | Glu | Glu | Glu | Gly | Val | Glu | Lys | Pro | Ala | Glu | Thr | His | Leu _. | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | |
| | TCG | GGG | AAA | ATT | GGA | GCT | AAG | AAA | CTG | CGG | AAG | CTG | GAG | GAG | AAA | CAA | 442 |
| | Ser | G1v | Lvs | Ile | Glv | Ala | Lvs | Lvs | Leu | Arg | Lvs | Leu | Glu | Glu | Lys | G1n | |

| | | 115 | | | | | 120 | | | | | 125 | | | | | |
|----|------|------|------|------|------|------|-------|------|-----|------|------|------|------|------|------|-------|------|
| | GCG | CGA | AAG | GCC | CAG | CGT | GAG | GCA | GAG | GAG | GCT | GAA | CGT | GAG | GAG | CGG | 490 |
| | Ala | Arg | Lys | Ala | G1n | Arg | Glu | Ala | Glu | Glu | Ala | Glu | Arg | Glu | Glu | Arg | • |
| | 130 | | | | | 135 | | | | | 140 | | | | | 145 | |
| 5 | AAA | CGA | CTC | GAG | TCC | CAG | CGC | GAA | GCT | GAG | TGG | AAG | AAG | GAG | GAG | GAG | 538 |
| | Lys | Arg | Leu | Glu | Ser | Gln | Arg | Glu | Ala | Glu | Trp | Lys | Lys | Glu | Glu | Glu | |
| | | | | | 150 | | | | | 155 | | | | | 160 | | |
| | CGG | CTT | CGC | CTG | GAG | GAG | GAG | CAG | AAG | GAG | GAG | GAG | GAG | AGG | AAG | GCC | 586 |
| | Arg | Leu | Arg | Leu | Glu | Glu | Glu | Gln | Lys | Glu | Glu | Glu | G1u | Arg | Lys | Ala | |
| 10 | | | | 165 | | | | | 170 | | | | | 175 | | | |
| | CGC | GAG | GAG | CAG | GCC | CAG | CGG | GAG | CAT | GAG | GAG | TAC | CTG | AAA | CTG | AAG | 634 |
| | Arg | Glu | Glu | Gln | Ala | Gln | Arg | Glu | His | Glu | G1u | Tyr | Leu | Lys | Leu | Lys | |
| | | | 180 | | | | | 185 | | | | | 190 | | | | |
| | GAG | GCC | TTT | GTG | GTG | GAG | GAG | GAA | GGC | GTA | GGA | GAG | ACC | ATG | ACT | GAG | 682 |
| 15 | Glu | Ala | Phe | Val | Val | Glu | Glu | Glu | Gly | Val | Gly | Glu | Thr | Met | Thr | Glu | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | |
| | GAA | CAG | TCC | CAG | AGC | TTC | CTG | ACA | GAG | TTC | ATC | AAC | TAC | ATC | AAG | CAG | 730 |
| | Glu | Gln | Ser | Gln | Ser | Phe | Leu | Thr | G1u | Phe | Ile | Asn | Tyr | Ile | Lys | Gln | |
| | 210 | | | | | 215 | | | | | 220 | | | | | 225 | |
| 20 | TCC | AAG | GTT | GTG | CTC | TTG | GAA | GAC | CTG | GCT | TCC | CAG | GTG | GGC | CTA | CGC | 778 |
| | Ser | Lys | Val | Val | Leu | Leu | Glu | Asp | Leu | Ala | Ser | Gln | Va1 | Gly | Leu | Arg | |
| | | | | | 230 | | | | | 235 | | | | | 240 | | |
| | ACT | CAG | GAC | ACC | ATA | AAT | CGC | ATC | CAG | GAC | CTG | CTG | GCT | GAG | GGG | ACT | 826 |
| | Thr | Gln | Asp | Thr | Ile | Asn | Arg | Ile | Gln | Asp | Leu | Leu | Ala | Glu | Gly | Thr | |
| 25 | | | | 245 | | | | | 250 | | | | | 255 | | | |
| | ATA | ACA | GGT | GTG | ATT | GAC | GAC | CGG | GGC | AAG | TTC | ATC | TAC | ATA | ACC | CCA | 874 |
| | Ile | Thr | G1y | Val | Ile | Asp | Asp | Arg | Gly | Lys | Phe | Ile | Tyr | Ile | Thr | Pro | |
| | | | 260 | | | | | 265 | | | | | 270 | | | | |
| | GAG | GAA | CTG | GCC | GCC | GTG | GCC . | AAC | TTC | ATC | CGA | CAG | CGG | GGC | CGG | GTG | 922 |
| 30 | G1u | Glu | Leu | Ala | Ala | Val | Ala | Asn | Phe | Ile | Arg | Gln | Arg | Gly | Arg | Val | |
| | | 275 | | | | | 280 | | | | | 285 | | | | | |
| | TCC | ATC | GCC | GAG | CTT | GCC | CAA | GCC | AGC | AAC | TCC | CTC | ATC | GCC | TGG | GGC | 970 |
| | Ser | Ile | Ala | Glu | Leu | Ala | Gln | Ala | Ser | Asn | Ser | Leu | Ile | Ala | Trp | Gly | |
| | 290 | | | | | 295 | | | | | 300 | | | | • | 305 | |
| 35 | CGG | GAG | TCC | CCT | GCC | CAA | GCC | CCA | GCC | TGAC | CCCA | GT C | CTTC | ССТС | т то | G | 1020 |
| | Arg | Glu | Ser | Pro | Ala | G1n | Ala | Pro | Ala | | | | | | | | |
| | | | | | 310 | | | | | | | | | | | | |
| | ACTO | AGAG | TT G | GTGT | GGCC | T AC | CTGG | CTAT | ACA | TCTT | CAT | CCCT | cccc | AC C | ATC | TGGGG | 1080 |

138

1131

AAGTGATGGT GTGGCCAGGC AGTTATAGAT TAAAGGCCTG TGAGTACTGC T

| | (2) INFO | RMATION | FOR SEQ | ID NO: | 46: | | | | | | | | | | |
|----|---|----------|----------|-----------|---------|------------|---------|--------|----------|-----|--|--|--|--|--|
| 5 | (i) SEQUENCE CHARACTERISTICS: | | | | | | | | | | | | | | |
| | (A) LENGTH: 1875 | | | | | | | | | | | | | | |
| | | (B) | TYPE: N | ucleic a | acid | | | | | | | | | | |
| | | (C) | STRANDE | DNESS: I | ouble | | | | | | | | | | |
| | | (D) | TOPOLOG | Y: Line | ır | | | | | | | | | | |
| 10 | (i | i) SEQU | ENCE KIN | D: cDNA | to mR | NA | | | | | | | | | |
| | | | | | | | | • | | | | | | | |
| | (v | i) ORIG | INAL SOU | RCE: | | | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| | | (B) | CELL KI | ND: Ston | nach ca | ancer | | | | | | | | | |
| 15 | (D) CLONE NAME: HP10413 | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| | (i | x) SEQUI | ENCE CHA | RACTERIS | TICS: | | | | | | | | | | |
| | • | (A) | CHARACT | ERIZATIO | N CODI | E: CDS | | | | | | | | | |
| | (B) EXISTENCE POSITION: 79 666 (C) CHARACTERIZATION METHOD: E | | | | | | | | | | | | | | |
| 20 | | (C) | CHARACT | ERIZATIO | N MET | HOD: E | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| | . (x | i) SEQUI | ENCE DES | CRIPTION | : SEQ | ID NO: | 46: | | | | | | | | |
| | CTCGCTCG | CT CAGAC | CCACC A | C | C CAC | የ ውር ር ር ር | TCCCTC(| CTA CC | GCGGCCCA | 60 | | | | | |
| 25 | ACCTTTAC | | | | | | | | | 111 | | | | | |
| | | | | Ala Ala | | | | | | *** | | | | | |
| | | | 1 | 1110 1110 | 014 / | 5 | var nie | | 10 | | | | | | |
| | GAC CCA | AGC GAT | | AGC GGC | GGG C | | CAT GAG | ATT T | | 159 | | | | | |
| | Asp Pro | | | | | | | | | | | | | | |
| 30 | | 15 | | | 20 | | | 25 | | | | | | | |
| | TCG CCG | CTC AAC | CTG CTG | CTG CTT | GGC C | TC TGC | ATC TTC | CTG C | TC TAC | 207 | | | | | |
| | Ser Pro | • | | | | | | | | | | | | | |
| | | 30 | | 35 | | | 40 | | | | | | | | |
| | AAG ATC | GTG CGC | GGG GAC | CAG CCG | GCG G | CC AGC | GGC GAC | AGC G | AC GAC | 255 | | | | | |
| 35 | Lys Ile ' | Val Arg | Gly Asp | Gln Pro | Ala A | la Ser | Gly Asp | Ser A | sp Asp | | | | | | |
| | 45 | | | 50 | | | 55 | | | | | | | | |
| | GAC GAG | cce ccc | CCT CTG | CCC CGC | CTC A | AG CGG | CGC GAC | TTC A | cc ccc | 303 | | | | | |

Asp Glu Pro Pro Pro Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro

| | - 60 | | | | | 65 | | | | | 70 | | | | | 75 | |
|----|------|--------|-------|-------|---------|------|--------|--------|------|------|-------------|------|--------|------|-------|-------|------|
| | GCC | GAG | CTG | CGG | CGC | TTC | GAC | GGC | GTC | CAG | GAC | CCG | CGC | ATA | CTC | ATG | 351 |
| | Ala | G1u | Leu | Arg | Arg | Phe | Asp | Gly | Val | Gln | Asp | Pro | Arg | Ile | Leu | Met | |
| | | | | | 80 | | | | | 85 | | | | | 90 | | |
| 5 | GCC | ATC | AAC | GGC | AAG | GTG | TTC | GAT | GTG | ACC | AAA | GGC | CGC | AAA | TTC | TAC | 399 |
| | Ala | Ile | Asn | Gly | Lys | Val | Phe | Asp | Val | Thr | Lys | Gly | Arg | Lys | Phe | Tyr | |
| | | | | 95 | | | | | 100 | | | | | 105 | | | |
| | GGG | ccc | GAG | GGG | CCG | TAT | GGG | GTC | TTT | GCT | GGA | AGA | GAT | GCA | TCC | AGG | 447 |
| | Gly | Pro | Glu | Gly | Pro | Tyr | Gly | Val | Phe | Ala | Gly | Arg | Asp | Ala | Ser | Arg | |
| 10 | | | 110 | | | | | 115 | | | | | 120 | | | | |
| | GGC | CTT | GCC | ACA | TTT | TGC | CTG | GAT | AAG | GAA | GCA | CTG | AAG | GAT | GAG | TAC | 495 |
| | Gly | Leu | Ala | Thr | Phe | Cys | Leu | Asp | Lys | Glu | Ala | Leu | Lys | Asp | Glu | Tyr | |
| | | 125 | | | | | 130 | | | | | 135 | | | | | |
| | GAT | GAC | CTT | TCT | GAC | CTC | ACT | GCT | GCC | CAG | CAG | GAG | ACT | CTG | AGT | GAC | 543 |
| 15 | Asp | Asp | Leu | Ser | Asp | Leu | Thr | Ala | Ala | Gln | Gln | Glu | Thr | Leu | Ser | Asp | |
| | 140 | | | | | 145 | | | | | 150 | | | | | 155 | |
| | TGG | GAG | TCT | CAG | TTC | ACT | TTC | AAG | TAT | CAT | CAC | GTG | GGC | AAA | CTG | CTG | 591 |
| | Trp | G1u | Ser | Gln | Phe | Thr | Phe | Lys | Tyr | His | His | Va1 | Gly | Lys | Leu | Leu | |
| | | | | | 160 | | | | | 165 | | | | | 170 | | |
| 20 | AAG | GAG | GGG | GAG | GAG | CCC | ACT | GTG | TAC | TCA | GAT | GAG | GAA | GAA | CCA | AAA | 639 |
| | Lys | Glu | Gly | Glu | Glu | Pro | Thr | Val | Tyr | Ser | Asp | Glu | Glu | Glu | Pro | Lys | |
| | | | | 175 | | | | | 180 | | | | | 185 | | | |
| | GAT | GAG | AGT | GCC | CGG | AAA | AAT | GAT | TAAA | GCAI | TC A | GTGG | AAGI | A TA | ATCTA | T | 690 |
| | Asp | Glu | Ser | Ala | Arg | Lys | Asn | Asp | | | | | | | | | |
| 25 | | | 190 | | | | | 195 | | | | | | | | | |
| | TTTI | GTA1 | TT T | rgcaa | AATC | IT A | TGTA | ACAG | TCC | ACTO | TGT | CTTI | 'AAAA' | CA 1 | CAGTG | ATTAC | 750 |
| | AATA | TTTA | AGA A | AGTI | TTGA | G CA | CTTG | CTAT | AAG | TTTI | TTA | TAAC | ATCA | CT A | GTGA | CACTA | 810 |
| | ATAA | LAAT? | C AA1 | CTTCI | TAGA | A TG | CATG | ATGT | GTT | TGTG | TGT | CACA | AATO | CA G | AAAG | TGAAC | 870 |
| | TGCA | GTGC | CTG 1 | ATAAT | CACA | T GI | raat' | ACTG | TTT | TTCI | TCT | ATCI | GTAG | TT A | GTAC | AGGAT | 930 |
| 30 | GAAI | 'ATTA | AAT G | STGTI | TTTC | C TG | AGAG | ACAA | GGA | AGAC | TTG | GGTA | TTTC | CC A | LAAAC | AGGTA | 990 |
| | AAAA | TCTI | AA? | ATGTG | CACC | A AG | AGCA | AAGG | ATC | AACT | TTT | AGTO | ATGA | TG T | TCTG | TAAAG | 1050 |
| | AÇAA | CAAA | ATC C | CTTI | TTTT | T TC | TCAA | TTGA | CTT | AACI | GCA | TGAT | TTCI | GT I | TATT | CTACC | 1110 |
| | TCTA | AAGC | CAA A | ATCTG | CAGT | G TI | 'CCAA | AGAC | TTT | GGTA | TGG | ATTA | AGCG | CT G | TCCA | GTAAC | 1170 |
| | AAAA | TGAA | AT C | CTCAA | AACA | G AG | CTCA | GCTG | CAA | AAAA | GCA | TATT | TTCI | GT G | TTTC | TGGAC | 1230 |
| 35 | | | | | | | | | | | | - | | | | GTCTA | 1290 |
| | | | | | | | | | | | | | | | | GCTGG | 1350 |
| | | | | | | | | | | | | | | | | CATGT | |
| | TCAT | יכפיים | വര വ | CAAT | יבכידים | Δ ΤΤ | יתכבית | ጥ ል ጥጥ | ጥጥ∆ | CTCA | ጥጥ ል | CCTT | ACTO | TC A | ጥጥፕር | AAATG | 1470 |

WO 98/55508 PCT/JP98/02445

AGGGAGGGAC ATACAGAATA GGAACAGGTG TTTGCTCTCC TAAGAGCCTT CATGCACACC 1530

| | CCTGAACCAC GAGGAAACAG TACAGTCGCT AGTCAAGTGG TTTTTAAAGT AAAGTATATT | 1590 |
|----|---|------|
| | CATAAGGTAA CAGTTATTCT GTTGTTATAA AACTATACCC ACTGCAAAAG TAGTAGTCAA | 1650 |
| | GTGTCTAGGT CTTTGATATT GCTCTTTTGG TTAACACTAA GCTTAAGTAG ACTATACAGT | 1710 |
| 5 | TGTATGAATT TGTAAAAGTA TATGAACACC TAGTGAGATT TCAAACTTGT AATTGTGGTT | 1770 |
| | AAATAGTCAT TGTATTTTCT TGTGAACTGT GTTTTATGAT TTTACCTCAA ATCAGAAAAC | 1830 |
| | AAAATGATGT GCTTTGGTCA GTTAATAAAA ATGGTTTTAC CCACT | 1875 |
| | | |
| • | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 47: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 1563 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 15 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | • |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| 20 | (B) CELL KIND: Stomach cancer | |
| | (D) CLONE NAME: HP10415 | |
| | • • | |
| | (ix) SEQUENCE CHARACTERISTICS: | |
| | (A) CHARACTERIZATION CODE: CDS | |
| 25 | (B) EXISTENCE POSITION: 72 1460 | |
| | (C) CHARACTERIZATION METHOD: E | |
| | | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47: | |
| _0 | | |
| 30 | AAATTGGGCC AGGCTGAGGC GCTGCTGCTG GAGCGGCCGA TCCGAGACGT GGCTCCCTGG | 60 |
| | GCGGCAGAAC C ATG TTG GAC TTC GCG ATC TTC GCC GTT ACC TTC TTG CTG | 110 |
| , | Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu | |
| | 1 5 10 | 158 |
| 35 | GCG TTG GTG GGA GCC GTG CTC TAC CTC TAT CCG GCT TCC AGA CAA GCT | 130 |
| 33 | Ala Leu Val Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala 15 20 25 | |
| | GCA GGA ATT CCA GGG ATT ACT CCA ACT GAA GAA AAA GAT GGT AAT CTT | 206 |
| | Ala Gly Ile Pro Gly Ile Thr Pro Thr Glu Glu Lys Asp Gly Asp Leu | |

| • | 30 | | | | | 35 | | | | | 40 | | | | | 45 | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | CCA | GAT | ATT | GTG | AAT | AGT | GGA | AGT | TTG | CAT | GAG | TTC | CTG | GTT | AAT | TTG | 254 |
| | Pro | Asp | Ile | Val | Asn | Ser | Gly | Ser | Leu | His | Glu | Phe | Leu | Val | Asn | Leu | |
| | | | | | 50 | | | | | 55 | | | | | 60 | | |
| 5 | CAT | GAG | AGA | TAT | GGG | CCT | GTG | GTC | TCC | TTC | TGG | TTT | GGC | AGG | CGC | CTC | 302 |
| | His | Glu | Arg | Tyr | Gly | Pro | Val | Val | Ser | Phe | Trp | Phe | Gly | Arg | Arg | Leu | |
| | | | | 65 | | | | | 70 | | | | | 75 | | | |
| | GTG | GTT | AGT | TTG | GGC | ACT | GTT | GAT | GTA | CTG | AAG | CAG | CAT | ATC | AAT | CCC | 350 |
| | Val | Val | Ser | Leu | Gly | Thr | Val | Asp | Val | Leu | Lys | Gln | His | Ile | Asn | Pro | |
| 10 | | | 80 | | | | | 85 | | | | | 90 | | | | |
| | AAT | AAG | ACA | TTG | GAC | CCT | TTT | GAA | ACC | ATG | CTG | AAG | TCA | TTA | TTA | AGG | 398 |
| | Asn | Lys | Thr | Leu | Asp | Pro | Phe | Glu | Thr | Met | Leu | Lys | Ser | Leu | Leu | Arg | • |
| | | 95 | | | | | 100 | | | | | 105 | | | | | |
| | TAT | CAA | TCT | GGT | GGT | GGC | AGT | GTG | AGT | GAA | AAC | CAC | ATG | AGG | AAA | AAA | 446 |
| 15 | Tyr | Gln | Ser | G1y | Gly | Gly | Ser | Val | Ser | Glu | Asn | His | Met | Arg | Lys | Lys | |
| | 110 | | | | | 115 | | | | • | 120 | | | | | 125 | |
| | TTG | TAT | GAA | AAT | GGT | GTG | ACT | GAT | TCT | CTG | AAG | AGT | AAC | TTT | GCC | CTC | 494 |
| | Leu | Tyr | Glu | Asn | Gly | Val | Thr | Asp | Ser | Leu | Lys | Ser | Asn | Phe | Ala | Leu | |
| | | • | | | 130 | | | | | 135 | | | | | 140 | | |
| 20 | CTC | CTA | AAG | CTT | TCA | GAA | GAA | TTA | TTA | GAT | AAA | TGG | CTC | TCC | TAC | CCA | 542 |
| | Leu | Leu | Lys | Leu | Ser | Glu | Glu | Leu | Leu | Asp | Lys | Trp | Leu | Ser | Tyr | Pro | |
| | | | | 145 | | | | | 150 | | | | | 155 | | | |
| | GAG | ACC | CAG | CAC | GTG | CCC | CTC | AGC | CAG | CAT | ATG | CTT | GGT | TTT | GCT | ATG | 590 |
| | Glu | Thr | Gln | His | Val | Pro | Leu | Ser | G1n | His | Met | Leu | Gly | Phe | Ala | Met | |
| 25 | | | 160 | | | | | 165 | | | | | 170 | | | | |
| | AAG | TCT | GTT | ACA | CAG | ATG | GTA | ATG | GGT | AGT | ACA | TTT | GAA | GAT | GAT | CAG | 638 |
| | Lys | Ser | Val | Thr | Gln | Met | Val | Met | Gly | Ser | Thr | Phe | Glu | Asp | Asp | Gln | |
| | | 175 | | | | | 180 | | | | | 185 | | | | | |
| | GAA | GTC | ATT | CGC | TTC | CAG | AAG | AAT | CAT | GGC | ACA | GTT | TGG | TCT | GAG | ATT | 686 |
| 30 | Glu | Val | Ile | Arg | Phe | Gln | Lys | Asn | His | Gly | Thr | Val | Trp | Ser | Glu | Ile | |
| | 190 | | | | | 195 | | | | | 200 | | | | | 205 | |
| | | | | | | | | | | | | | ATG | | | | 734 |
| | Gly | Lys | Gly | Phe | Leu | Asp | Gly | Ser | Leu | Asp | Lys | Asn | Met | Thr | Arg | Lys | |
| | | | | | 210 | | | | | 215 | | | | | 220 | | |
| 35 | | | | | | | | | | | | | GTT | | | | 782 |
| | Lys | Gln | Tyr | Glu | Asp | Ala | Leu | Met | Gln | Leu | Glu | Ser | Val | | Arg | Asn | |
| | | | | 225 | | | | | 230 | | | | | 235 | | | |
| | ATC | ATA | AAA | GAA | CGA | AAA | GGA | AGG | AAC | TTC | AGT | CAA | CAT | ATT | TTC | ATT | 830 |

| | Ile | Ile | | Glu | Arg | Lys | Gly | | Asn | Phe | Ser | Gln | | Ile | Phe | Ile | , |
|----|------------------|-------|--------|------------|------|------|--------|------|-----|---------|-----|-----|---------|------|-------|-------------|------|
| | | | 240 | | | | | 245 | | | | | 250 | | | | |
| | | | | | | | | | | | | | | | | GAC | 878 |
| - | Asp | | Leu | Val | GIn | GLy | | Leu | Asn | Asp | Gln | | TTe | Leu | Glu | Asp | |
| 5 | | 255 | 4 10 4 | mmm | mo.m | 0.00 | 260 | | | | | 265 | 004 | | mmo. | mom | 006 |
| | | | | TTT | | | | | | | | | | | | | 926 |
| | | met | TTE | Phe | Ser | | ALA | Ser | Cys | IIe | | Thr | ALB | гÀг | Leu | | |
| | 270 | maa | 004 | A M Č | mom | 275 | mm A | 400 | 400 | mom | 280 | | 0.00m | 044 | A A A | 285 | 07/ |
| 10 | | | | ATC | | | | | | | | | | | | | 974 |
| 10 | Thr | Trp | AIA | Ile | _ | Pne | Leu | Thr | Thr | | GIU | GIU | val | Gin | | ràs | |
| | | m . m | | 040 | 290 | 440 | | 0.00 | | 295 | | 00m | 000 | 0.00 | 300 | 004 | 1000 |
| | | | | GAG | | | | | | | | | | | | | 1022 |
| | Leu | Tyr | GIU | G1u 305 | 116 | ASII | GIN | VAI | | GIY | Asn | GIY | Pro | 315 | ini | PIO | |
| 15 | CAC | A A A | ለ ጥ ጥ | GAG | CAC | CTC | A.C. A | ጥለጥ | 310 | CAC | CAT | CTC | C TP TP | | CAA | ለ C TT | 1070 |
| 13 | | | | Glu | | | | | | | | | | | | | 1070 |
| | GIG | руз | 320 | Giu | GIII | Leu | MI B | 325 | Cys | GIII | птэ | VAI | 330 | cys | Giu | 1111 | |
| | ርጥጥ | CGA | | GCC | ΔΔΔ | CTG | ልሮሞ | | ርጥጥ | un C un | ccc | CAG | | CAA | САТ | Δ ΨΨ | 1118 |
| | | | | Ala | | | | | | | | | | | | | 1110 |
| 20 | | 335 | | | _, . | | 340 | | ,,, | 001 | | 345 | 200 | 02 | | | |
| | GAA | | AAA | ATT | GAC | CGA | | ATT | ATT | ССТ | AĠA | | ACC | CTC | GTC | CTT | 1166 |
| | _ | | | Ile | | | | | | | | | | | | | |
| | 350 ⁻ | • | • | | • | 355 | | | | | 360 | | | | | 365 | |
| | TAT | GCC | CTT | GGT | GTG | GTA | CTT | CAG | GAT | CCT | AAT | ACT | TGG | CCA | TCT | CCA | 1214 |
| 25 | | | | G1y | | | | | | | | | | | | | |
| | Ū | | | • | 370 | | | | - | 375 | | | - | | 380 | | |
| | CAC | AAG | TTT | GAT | CCA | GAT | CGG | TTT | GAT | GAT | GAA | TTA | GTA | ATG | AAA | ACT | 1262 |
| | His | Lys | Phe | Asp | Pro | Asp | Arg | Phe | Asp | Asp | Glu | Leu | Va1 | Met | Lys | Thr | |
| | | | | 385 | | | | | 390 | | | | | 395 | | | |
| 30 | TTT | TCC | TCA | CTT | GGA | TTC | TCA | GGC | ACA | CAG | GAG | TGT | CCA | GAG | TTG | AGG | 1310 |
| | Phe | Ser | Ser | Leu | Gly | Phe | Ser | Gly. | Thr | Gln | Glu | Cys | Pro | Glu | Leu | Arg | |
| | | | 400 | | | | | 405 | | | | | 410 | | | | |
| | TTT | GCA | TAT | ATG | GTG | ACC | ACA | GTA | CTT | CTT | AGT | GTA | TTG | GTG | AAG | AGA | 1358 |
| | Phe | Ala | Tyr | Met | Val | Thr | Thr | Val | Leu | Leu | Ser | Val | Leu | Val | Lys | Arg | |
| 35 | | 415 | | | | | 420 | | | | | 425 | | | | | |
| | CTG | CAC | CTA | CTT | TCT | GTG | GAG | GGA | CAG | GTT | ATT | GAA | ACA | AAG | TAT | GAA | 1406 |
| | Leu | His | Leu | Leu | Ser | Val | Glu | Gly | Gln | Val | Ile | Glu | Thr | Lys | Tyr | Glu | |
| | 430 | | | | | 435 | | | | | 440 | | | | | 445 | |

| | CTG GTA ACA TCA AGG GAA GAA GCT TGG ATC ACT GTC TCA AAG AGA | 145 |
|----|---|--------------|
| | Leu Val Thr Ser Ser Arg Glu Glu Ala Trp Ile Thr Val Ser Lys Arg | |
| | 450 455 460 | |
| | TAT TAAAATTTTA TACATTTAAA ATCATTGTTA AATTGATTGA GGAAAACAAC CAT | 151 |
| 5 | Tyr | |
| | | |
| | TTAAAAAAAA TCTATGTTGA ATCCTTTTAT AAACCAGTAT CACTTTGTAA TAT | 1563 |
| | | |
| | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 48: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 2030 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 15 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | • |
| | | |
| · | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| 20 | (B) CELL KIND: Stomach cancer | |
| | (D) CLONE NAME: HP10419 | |
| | | |
| | (ix) SEQUENCE CHARACTERISTICS: | |
| 25 | (A) CHARACTERIZATION CODE: CDS | |
| 25 | (B) EXISTENCE POSITION: 171 914 | |
| | (C) CHARACTERIZATION METHOD: E | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48: | |
| | (XI) DEGOEAGE DESCRIPTION: SEQ ID NO. 40. | |
| 30 | CATTTGGGGT TTCGGTTCCC CCCCTTCCCC TTCCCCGGGG TCTGGGGGTG ACATTGCACC | 60 |
| | GCGCCCTCG TGGGGTCGCG TTGCCACCCC ACGCGGACTC CCCAGCTGGC GCGCCCCTCC | 120 |
| | CATTTGCCTG TCCTGGTCAG GCCCCCACCC CCCTTCCCAC CTGACCAGCC ATG GGG | 176 |
| | Met Gly | 2,0 |
| | 1 | |
| 35 | GCT GCG GTG TTT TTC GGC TGC ACT TTC GTC GCG TTC GGC CCG GCC TTC | 224 |
| • | Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro Ala Phe | _ _ . |
| | 5 10 15 | |
| | GCG CTT TTC TTG ATC ACT GTG GCT GGG GAC CCG CTT CGC GTT ATC ATC | 272 |
| | - / | |

| | Ala | Leu | Phe | Leu | Ile | Thr | Va1 | Ala | Gly | Asp | Pro | Leu | Arg | Val | Ile | Ile | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 20 | | | | | 25 | | | | | 30 | | | | | |
| | CTG | GTC | GCA | GGG | GCA | TTT | TTC | TGG | CTG | GTC | TCC | CTG | CTC | CTG | GCC | TCT | 320 |
| | Leu | Val | Ala | Gly | Ala | Phe | Phe | Trp | Leu | Val | Ser | Leu | Leu | Leu | Ala | Ser | |
| 5 | 35 | | | | | 40 | | | | | 45 | | | | | 50 | |
| | GTG | GTC | TGG | TTC | ATC | TTG | GTC | CAT | GTG | ACC | GAC | CGG | TCA | GAT | GCC | CGG | 368 |
| | Val | Val | Trp | Phe | Ile | Leu | Val | His | Val | Thr | Asp | Arg | Ser | Asp | Ala | Arg | |
| | | | | | 55 | | | | | 60 | | | | | 65 | | |
| | CTC | CAG | TAC | GGC | CTC | CTG | ATT | TTT | GGT | GCT | GCT | GTC | TCT | GTC | CTT | CTA | 416 |
| 10 | Leu | Gln | Tyr | Gly | Leu | Leu | Ile | Phe | Gly | Ala | Ala | Val | Ser | Val | Leu | Leu | |
| | | | | 70 | | | | | 75 | | | | | 80 | | | |
| | CAG | GAG | GTG | TTC | CGC | TTT | GCC | TAC | TAC | AAG | CTG | CTT | AAG | AAG | GCA | GAT | 464 |
| | Gln | Glu | Val | Phe | Arg | Phe | Ala | Tyr | Tyr | Lys | Leu | Leu | Lys | Lys | Ala | Asp | |
| | | | 85 | | | | | 90 | | | | | 95 | | | | |
| 15 | GAG | GGG | TTA | GCA | TCG | CTG | AGT | GAG | GAC | GGA | AGA | TCA | CCC | ATC | TCC | ATC | 512 |
| | Glu | Gly | Leu | Ala | Ser | Leu | Ser | Glu | Asp | Gly | Arg | Ser | Pro | Ile | Ser | Ile | |
| | | 100 | | | | | 105 | | | | | 110 | | | | | |
| | CGC | CAG | ATG | GCC | TAT | GTT | TCT | GGT | CTC | TCC | TTC | GGT | ATC | ATC | AGT | GGT | 560 |
| | Arg | Gln | Met | Ala | Tyr | Va1 | Ser | Gly | Leu | Ser | Phe | Gly | Ile | Ile | Ser | Gly | |
| 20 | 115 | | | | | 120 | | | | | 125 | | | | | 130 | |
| | GTC | TTC | TCT | GTT | ATC | TAA | ATT | TTG | GCT | GAT | GCA | CTT | GGG | CCA | GGT | GTG | 608 |
| | Val | Phe | Ser | Val | Ile | Asn | Ile | Leu | Ala | Asp | Ala | Leu | Gly | Pro | Gly | Val | |
| | | | | | 135 | | | | | 140 | | | | | 145 | | |
| | | | | | | GAC | | | | | | | | | | | 656 |
| 25 | Val | Gly | Ile | His | Gly | Asp | Ser | Pro | Tyr | Tyr | Phe | Leu | Thr | Ser | Ala | Phe | |
| | | | | 150 | | | | | 155 | | | | | 160 | | | |
| | | | | | | ATC | | | | | | | | | | | 704 |
| | Leu | Thr | | Ala | Ile | Ile | Leu | Leu | His | Thr | Phe | Trp | Gly | Val | Val | Phe | |
| | | | 165 | | | | | 170 | | | | | 175 | | | | |
| 30 | | | | | | AGG | | | | | | | | | | | 752 |
| | Phe | | Ala | Cys | Glu | Arg | - | Arg | Tyr | Trp | Ala | | Gly | Leu | Val | Val | |
| | | 180 | | | | | 185 | | | | | 190 | | | | | |
| | | | | | | ACA | | | | | | | | | | | 800 |
| 2.5 | | Ser | His | Leu | Leu | Thr | Ser | Gly | Leu | Thr | | Leu | Asn | Pro | Trp | | |
| 35 | 195 | | | | | 200 | | | | | 205 | | | | | 210 | |
| | | | | | | CCC | | | | | | | | | | | 848 |
| | Glu | Ala | Ser | Leu | | Pro | Ile | Tyr | | | Thr | Val | Ser | Met | _ | Leu | |
| | | | | | 215 | | | | | 220 | | | | | 225 | | |

145

| | TGG GCC TTC ATC ACA | GCT GGA GGG | TCC CTC CGA | AGT ATT CAG C | GC AGC 896 |
|-----|---------------------|----------------|-------------|----------------|---------------|
| | Trp Ala Phe Ile Th | Ala Gly Gly | Ser Leu Arg | Ser Ile Gln A | rg Ser |
| | 230 | | 235 | 240 | |
| | CTC TTG TGT AAG GAG | TGACTACCTG G | ACTGATCGC C | GACAGATC CCAC | CTGCC 950 |
| 5 | Leu Leu Cys Lys Asp |) | | | |
| | 245 | | | | |
| | TGTCCACTGC CCATGAC | GA GCCCAGCCC | AGCCCGGGTC | CATTGCCCAC AT | TCTCTGTC 1010 |
| | TCCTTCTCGT CGGTCTAC | CC CACTACCTCC | AGGGTTTTGC | TTTGTCCTTT TG | TGACCGTT 1070 |
| | AGTCTCTAAG CTTTACCA | .gg Agcagcctgg | GTTCAGCCAG | TCAGTGACTG GT | GGGTTTGA 1130 |
| 10 | ATCTGCACTT ATCCCCAC | CA CCTGGGGACC | CCCTTGTTGT | GTCCAGGACT CC | CCCTGTGT 1190 |
| | CAGTGCTCTG CTCTCACC | CT GCCCAAGACT | CACCTCCCTT | CCCCTCTGCA GG | CCGACGGC 1250 |
| | AGGAGGACAG TCGGGTGA | TG GTGTATTCTG | CCCTGCGCAT | CCCACCGAG GAG | CTGAGGGA 1310 |
| | ACCTAGGGGG GACCCCTO | GG CCTGGGGTGC | CCTCCTGATG | TCCTCGCCCT GT | ATTTCTCC 1370 |
| | ATCTCCAGTT CTGGACAC | TG CAGGTTGCCA | AGAAAAGGGA | CCTAGTTTAG CCA | ATTGCCCT 1430 |
| 1.5 | GGAGATGAAA TTAATGGA | | | | · |
| | AAGACTGGAC ATCTTGGT | CT TTTTCTCAGG | CCTGAGGGG | AACCATTTT GG | IGTGATAA 1550 |
| | ATACCCTAAA CTGCCTT | | | | |
| | CTCTTCTAAC CTCCTTG | | | | |
| | ATTTCGGTCC CTTTCTCC | | | | |
| 20 | GGAACTGGCA TTACTGGA | AC TAATGGTTTT | AACCTCCTTA | ACCACCAGCA TC | CCTCCTCT 1790 |
| | CCCCAAGGTG AAGTGGAG | | | | |
| | GGAGGAGTCA GACTACCA | TG ACATCGTAGG | GAAGGAGGGG | AGATTTTTT GT | AGTTTTTA 1910 |
| • | ATTGGGGTGT GGGAGGG | CG GGGAGGTTTT | CTATAAACTG | TATCATTTTC TG | CTGAGGGT 1970 |
| | GGAGTGTCCC ATCCTTT | | | | |
| 25 | | · | | | |
| | | | | | |

(2) INFORMATION FOR SEQ ID NO: 49:

- (1) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 493
- 30 (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
- 35 (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10424

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(ix) SEQUENCE CHARACTERISTICS:

(1) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2044

| | (A) CHARACTERIZATION CODE: CDS (B) EXISTENCE POSITION: 98 439 | | | | | | | | | | | | | | | | |
|----|--|------|-------|------|-------|------|------|-------|-------|-------|------|------|------|------|------|--------|-----|
| | | | | (B) | EXI | STEN | CE P | OSIT | ION: | 98. | . 43 | 9 | | : | | | |
| | | | | (C) | CHA | RACT | ERIZ | ATIO | N ME | THOD | : E | | | | | | |
| 5 | | | | | | | | | | | | | | | | | |
| | | (| xi) | SEQU | ENCE | DES | CRIP | TION | : SE | Q ID | NO: | 49: | | | | | |
| | | | | | | | | | | | | | | | | | |
| | AAA | GTTT | CCC . | AAAT | CCAG | GC G | GCTA | GAGG | c cc. | ACTG | CTTC | CCA | ACTA | CCA | GCTG | AGGGGG | 60 |
| | TCC | GTCC | CGA | GAAG | GGAG. | AA G | AGGC | CGAA | G AG | GAAA | C AT | G AA | с тт | C TA | т тт | A CTC | 115 |
| 10 | | | | | | | | | | | Ме | t As | n Ph | е Ту | r Le | u Leu | |
| | | | | | | | | | | | | 1 | | | • | 5 | |
| | CTA | GCG | AGC | AGC | ATT | CTG | TGT | GCC | TTG | ATT | GTC | TTC | TGG | AAA | TAT | CGC | 163 |
| | Leu | Ala | Ser | Ser | Ile | Leu | Cys | Ala | Leu | Ile | Val | Phe | Trp | Lys | Tyr | Arg | |
| | | | | 10 | | | | | 15 | | | | | 20 | | | |
| 15 | CGC | TTT | CAG | AGA | AAC | ACT | GGC | GAA | ATG | TCA | TCA | AAT | TCA | ACT | GCT | CTT | 211 |
| | Arg | Phe | Gln | Arg | Asn | Thr | Gly | Glu | Met | Ser | Ser | Asn | Ser | Thr | Ala | Leu | |
| | | | 25 | | | | | 30 | | | | | 35 | | | | |
| | GCA | CTA | GTG | AGA | ССС | TCT | TCT | TCT | GGG | TTA | ATT | AAC | AGC | AAT | ACA | GAC | 259 |
| | Ala | Leu | Val | Arg | Pro | Ser | Ser | Ser | Gly | Leu | Ile | Asn | Ser | Asn | Thr | Asp | |
| 20 | | 40 | | | | | 45 | | _ | | | 50 | | | | | |
| | AAC | AAT | CTT | GCA | GTC | TAC | GAC | CTC | TCT | CGG | GAT | ATT | TTA | AAT | AAT | TTC | 307 |
| | Asn | Asn | Leu | Ala | Val | Tyr | Asp | Leu | Ser | Arg | Asp | Ile | Leu | Asn | Asn | Phe | |
| | 55 | | | | | 60 | _ | | | Ū | 65 | | | | | 70 | |
| | CCA | CAC | TCA | ATA | GCC | AGG | CAG | AAG | CGA | ATA | TTG | GTA | AAC | CTC | AGT | ATG | 355 |
| 25 | | | | | | | | | | | | | | | Ser | | |
| | | | | | 75 | | • | | | 80 | | | | | 85 | | |
| | GTG | GAA | AÁC | AAG | CTG | GTT | GAA | CTG | GAA | CAT | ACT | CTA | CTT | AGC | AAG | GGT | 403 |
| | Va1 | Glu | Asn | Lys | Leu | Val | Glu | Leu | Glu | His | Thr | Leu | Leu | Ser | Lys | Gly | |
| | | | | 90 | | | | | 95 | | | | • | 100 | | | |
| 30 | TTC | AGA | GGT | GCA | TCA | CCT | CAC | CGG | AAA | TCC | ACC | TAAA | AGC | TA (| CAGG | | 450 |
| • | Phe | Arg | Gly | Ala | Ser | Pro | His | Arg | Lys | Ser | Thr | | | • | | | |
| | | | 105 | | | | | 110 | | | | | | | | | |
| | ATGI | 'AAT | SCC A | GTGG | TGGA | A A | CATI | `AAAG | AC | CACTI | TGA | GTAG | ; | | | | 493 |
| | | | | | | | | | | | | | | | | | |
| 35 | | | | | | | | | | | | | | | | | |
| | (2) | INFO | RMAT | CION | FOR | SEQ | ID N | 10: 5 | 0: | | | | | | | | |

| | (B) TYPE: Nucleic acid | |
|----|---|-----|
| | (C) STRANDEDNESS: Double | |
| | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| 5 | | |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| | (B) CELL KIND: Epidermoid carcinoma | |
| | (C) CELL LINE: KB | |
| 10 | (D) CLONE NAME: HP10428 | |
| | | |
| | (ix) SEQUENCE CHARACTERISTICS: | |
| | (A) CHARACTERIZATION CODE: CDS | |
| | (B) EXISTENCE POSITION: 288 1385 | |
| 15 | (C) CHARACTERIZATION METHOD: E | |
| | | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50: | |
| | | |
| 20 | AGATTCCGGC CTGGAGCTCC CAGGGCCGAG CAGACCTTGG GACCTGTGAG CGCTGCATCC | 60 |
| 20 | AATTAACCAT GGGAAGGGTC AGCACCAGCC ACCAGCCCCT TAGGTGAGGA CTCTGCCTGG | 120 |
| | GGCTCTGCTG ATGGTTCCGA ATCATGGAGC TGCAGAGAGC TCCTCCAGCC TGGAGACGTT | 180 |
| | CTTGGTGAAA GCTGTGGTCT AACTCCACCG GCTCTTCCTG CACATTGTAT TCAAGAGGGG TGCCTGCCCC CGCTGACTCA GGAGCTCCGG TGCTGCAGCC GCCACGA ATG GGG AGG | 240 |
| | Met Gly Arg | 250 |
| 25 | 1 | |
| | TGG GCC CTC GAT GTG GCC TTT TTG TGG AAG GCG GTG TTG ACC CTG GGG | 344 |
| | Trp Ala Leu Asp Val Ala Phe Leu Trp Lys Ala Val Leu Thr Leu Gly | 31, |
| | 5 10 15 | |
| | CTG GTG CTT CTC TAC TAC TGC TTC TCC ATC GGC ATC ACC TTC TAC AAC | 392 |
| 30 | Leu Val Leu Leu Tyr Tyr Cys Phe Ser Ile Gly Ile Thr Phe Tyr Asn | |
| | 20 25 30 35 | |
| | AAG TGG CTG ACA AAG AGC TTC CAT TTC CCC CTC TTC ATG ACG ATG CTG | 440 |
| | Lys Trp Leu Thr Lys Ser Phe His Phe Pro Leu Phe Met Thr Met Leu | |
| | 40 45 50 | |
| 35 | CAC CTG GCC GTG ATC TTC CTC TTC TCC GCC CTG TCC AGG GCG CTG GTT | 488 |
| | His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser Arg Ala Leu Val | |
| | 55 60 65 | |
| | CAG TGC TCC AGC CAC AGG GCC CGT GTG GTG CTG AGC TGG GCC GAC TAC | 536 |

| | Gln | Cys | Ser | Ser | His | Arg | Ala | Arg | Val | Val | Leu | Ser | Trp | Ala | Asp | Tyr | • |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|------|
| | | | 70 | | | | | 75 | | | | | 80 | | | | |
| | CTC | AGA | AGA | GTG | GCT | ccc | ACA | GCT | CTG | GCG | ACG | GCG | CTT | GAC | GTG | GGC | 584 |
| | Leu | Arg | Arg | Val | Ala | Pro | Thr | Ala | Leu | Ala | Thr | Ala | Leu | Asp | Val | Gly | |
| 5 | | 85 | | | | | 90 | | | | | 95 | | | | | |
| | TTG | TCC | AAC | TGG | AGC | TTC | CTG | TAT | GTC | ACC | GTC | TCG | CTG | TAC | ACA | ATG | 632 |
| | Leu | Ser | Asn | Trp | Ser | Phe | Leu | Tyr | Val | Thr | Val | Ser | Leu | Tyr | Thr | Met | |
| | 100 | | | | | 105 | | | | | 110 | | | | | 115 | |
| | ACC | AAA | TCC | TCA | GCT | GTC | CTC | TTC | ATC | TTG | ATC | TTC | TCT | CTG | ATC | TTC | 680 |
| 10 | Thr | Lys | Ser | Ser | Ala | Va1 | Leu | Phe | Ile | Leu | Ile | Phe | Ser | Leu | Ile | Phe | |
| | | | | | 120 | | | | | 125 | | | | | 130 | | |
| • | AAG | CTG | GAG | GAG | CTG | CGC | GCG | GCA | CTG | GTC | CTG | GTG | GTC | CTC | CTC | ATC | 728 |
| | Lys | Leu | Glu | Glu | Leu | Arg | Ala | Ala | Leu | Val | Leu | Val | Val | Leu | Leu | Ile | |
| | | | | 135 | | | | | 140 | | | | | 145 | | | |
| 15 | GCC | GGG | GGT | CTC | TTC | ATG | TTC | ACC | TAC | AAG | TCC | ACA | CAG | TTC | AAC | GTG | 776 |
| | Ala | Gly | Gly | Leu | Phe | Met | Phe | Thr | Tyr | Lys | Ser | Thr | Gln | Phe | Asn | Val | |
| | | | 150 | | | | | 155 | | | | | 160 | | | | |
| | GAG | GGC | TTC | GCC | TTG | GTG | CTG | GGG | GCC | TCG | TTC | ATC | GGT | GGC | ATT | CGC | 824 |
| | G1u | G1y | Phe | Ala | Leu | Val | Leu | Gly | Ala | Ser | Phe | Ile | Gly | Gly | Ile | Arg | |
| 20 | | 165 | | | • | | 170 | | | | | 175 | | | | | |
| | TGG | ACC | CTC | ACC | CAG | ATG | CTC | CTG | CAG | AAG | GCT | GAA | CTC | GGC | CTC | CAG | 872 |
| | Trp | Thr | Leu | Thr | Gln | Met | Leu | Leu | Gln | Lys | Ala | Glu | Leu | Gly | Leu | Gln | |
| | 180 | | | | | 185 | | | | | 190 | | | | | 195 | |
| | AAT | ccc | ATC | GAC | ACC | ATG | TTC | CAC | CTG | CAG | CCA | CTC | ATG | TTC | CTG | GGG | 920 |
| 25 | Asn | Pro | Ile | Asp | Thr | Met | Phe | His | Leu | Gl'n | Pro | Leu | Met | Phe | Leu | Gly | |
| | | | | | 200 | | | | | 205 | | | | | 210 | | |
| | CTC | TTC | CCT | CTC | TTT | GCT | GTA | TTT | GAA | GGT | CTC | CAT | TTG | TCC | ACA | TCT | 968 |
| | Leu | Phe | Pro | Leu | Phe | Ala | Val | Phe | Glu | Gly | Leu | His | Leu | Ser | Thr | Ser | |
| | | • | | 215 | | | | | 220 | | | | | 225 | | | |
| 30 | GAG | AAA | ATC | TTC | CGT | TTC | CAG | GAC | ACA | GGG | CTG | CTC | CTG | CGG | GTA | CTT | 1016 |
| ٠ | G1u | Lys | Ile | Phe | Arg | Phe | G1n | Asp | Thr | Gly | Leu | Leu | Leu | Arg | Val | Leu | |
| | | | 230 | | | | | 235 | | | | | 240 | | | | |
| | GGG | AGC | CTC | TTC | CTT | GGC | GGG | ATT | CTC | GCC | TTT | GGT | TTG | GGC | TTC | TCT | 1064 |
| | Gly | Ser | Leu | Phe | Leu | Gly | Gly | Ile | Leu | Ala | Phe | Gly | Leu | Gly | Phe | Ser | |
| 35 | | 245 | | | | | 250 | | | | | 255 | | | | | |
| | GAG | TTC | CTC | CTG | GTC | TCC | AGA | ACC | TCC | AGC | CTC | ACT | CTC | TCC | TTA | GCC | 1112 |
| | Glu | Phe | Leu | Leu | Val | Ser | Arg | Thr | Ser | Ser | Leu | Thr | Leu | Ser | Ile | Ala | |
| | 260 | | | | | 265 | | | | | 270 | | | | | 275 | |

149

| | GGC | ATT | TTT | AAG | GAA | GTC | TGC | ACT | TTG | CTG | TTG | GCA | GCT | CAT | CTG | CTG | 1160 |
|----|------|-------|-------|-------|-------|------|-------|------|-----|-------|------|------|-------|-------|------|-------|------|
| | Gly | Ile | Phe | Lys | Glu | Val | Cys | Thr | Leu | Leu | Leu | Ala | Ala | His | Leu | Leu | |
| | | | | | 280 | | | | | 285 | | | | | 290 | | |
| | GGC | GAT | CAG | ATC | AGC | CTC | CTG | AAC | TGG | CTG | GGÇ | TTC | GCC | CTC | TGC | CTC | 1208 |
| 5 | Gly | Asp | Gln | Ile | Ser | Leu | Leu | Asn | Trp | Leu | G1y | Phe | Ala | Leu | Cys | Leu | |
| | | | | 295 | | | | | 300 | | | | | 305 | | | |
| | TCG | GGA | ATA | TCC | CTC | CAC | GTT | GCC | CTC | AAA | GCC | CTG | CAT | TCC | AGA | GGT | 1256 |
| | Ser | Gly | Ile | Ser | Leu | His | Val | Ala | Leu | Lys | Ala | Leu | His | Ser | Arg | Gly | |
| | | | 310 | | | | | 315 | | | | | 320 | | | | |
| 10 | GAT | GGT | GGC | ccc | AAG | GCC | TTG | AAG | GGG | CTG | GGC | TCC | AGC | ccc | GAC | CTG | 1304 |
| | Asp | Gly | Gly | Pro | Lys | Ala | Leu | Lys | Gly | Leu | Gly | Ser | Ser | Pro | Asp | Leu | |
| | | 325 | | | | | 330 | | | | | 335 | | | | | |
| | GAG | CTG | CTG | CTC | CGG | AGC | AGĊ | CAG | CGG | GAG | GAA | GGT | GAC | AAT | GAG | GAG | 1352 |
| | Glu | Leu | Leu | Leu | Arg | Ser | Ser | Gln | Arg | Glu | Glu | Gly | Asp | Asn | Glu | Glu | |
| 15 | 340 | | | | | 345 | | | | | 350 | | | | | 355 | |
| | GAG | GAG | TAC | TTT | GTG | GCC | CAG | GGG | CAG | CAG | TGAC | CAGC | CA G | GGCA | TAA | | 1400 |
| | Glu | G1u | Tyr | Phe | Val | Ala | Gln | Gly | Gln | Gln | | | | | | | |
| | | | | | 360 | | | | | 365 | | | | | | | |
| | GGC | TAGA | AAG (| CAGGO | CACI | c cc | CAGC | CTGC | TGC | CAGO | CACT | CACI | GTGC | TC A | AGCC | GCCAG | 1460 |
| 20 | GGC | CATO | CAT | GTAG | CTGG | G AG | CTGI | GGAC | GGG | AGTO | CACC | AGGI | GGTG | GG G | CCAA | GCCAG | 1520 |
| | GGA | CTCAT | rga (| CTTTI | recco | C TC | CCTI | CAGA | GCC | TGGT | CAC | ACAA | .GGGG | CG A | GCAC | CAGGC | 1580 |
| | CAG | CTGG | GA (| CTGGC | CAGA | G CI | 'GGGC | CCAA | GCI | 'GCGC | TGG | AATC | GCAG | CA G | GAGA | GGGGA | 1640 |
| | GTGG | GCT | GT 1 | CTTC | CCAC | C AC | TTCC | CAGG | CTC | TGAC | AGC | CGAG | ACTO | AT T | TCCA | AGGCA | 1700 |
| | CAG | CAGCI | TTT (| AAAT | AGGGA | C TG | AGTI | TGGA | CTG | GGTT | TTG | GACC | TCCA | .GG G | GCTG | GAGCT | 1760 |
| 25 | TCAT | CACC | TG G | GCAG | TGTC | T TI | TCTC | AGAG | AGC | AGGT | TTC | TTTA | TAGT | TT G | GAAA | TAAAT | 1820 |
| | GGTI | CACG | GT (| CACT | GGCC | G CC | TTGT | GTTG | CTG | GAGA | CGT | GGGG | GCAG | GG A | GGGG | ACAGT | 1880 |
| | GTG | GCCI | 'GG C | CTCI | CCTI | T CC | TTTC | CCTG | CCI | GGAG | CCT | TCTT | CAAA | TG T | CTGG | TCTTA | 1940 |
| | AGC | CAGGO | CT C | CTTC | TTTA | T CT | CGCT | CCTG | TTA | GAAC | ACC | AGTC | CCCT | cc c | CAGT | GGGGC | 2000 |
| | CCCA | CTGC | CAC C | TGCI | GGCA | G GA | ATAA | AATG | AAT | GTTT | ACT | GAGT | | | | | 2044 |
| 30 | | | | | | | | | | | | | | | | | |

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1043

(B) TYPE: Nucleic acid

35

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

WO 98/55508

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

| | | | | (B) | CEL | L KI | ND: | Ston | ach | canc | er | | | | | • | |
|----|-------|---------|-------|-----------|-----------|--------------|-------|--------|------|------|------|-------|------|-------|------|--------|-----|
| | | | | (D) | CLO | NE N | IAME: | HP1 | 0429 |) | | | | | | | |
| 5 | | | | | | | | | | | | | | | | | |
| | | (| ix) | SEQU | ENCE | СНА | RACT | ERIS | TICS | : | | | | | | | |
| | | | | (A) | СНА | RACT | ERIZ | ATIO | N CO | DE: | CDS | | | | | | |
| | | | | (B) | EXI | STEN | CE P | OSIT | ION: | 157 | 8 | 37 | | | | | |
| | | | | (C) | СНА | RACT | ERIZ | ATIO | n me | THOD | : E | | | | | | |
| 10 | | | | | | | | | | | | | | | • | | |
| | | (| xi) | SEQU | ENCE | DES | CRIP | TION | : SE | Q ID | NO: | 51: | | | | | |
| • | | | | | | | | | | | | | | | | | |
| | ATT | AGCA | TAA | CCCT | TCCT | CA G | GAAG | AGTG | A GA | TTTT | ATAT | TTG | ACAA | TAA | AGTG | TTAGAC | 60 |
| | TCC | ATTT | CTA . | AATA | CCAG | AC T | TCAA | AAGA | T AA | GGTT | CAAA | AGT | GTTA | TAA | GAAG | ATATTC | 120 |
| 15 | CTT | TTTT | TGT | CCTA | GAGA | AC T | TATT | TTCC | T GT | GAAA | ATG | CCT | ACC | ACA | AAG | AAG | 174 |
| | | | | | | | | | | | Met | Pro | Thr | Thr | Lys | Lys | |
| | | | | | | | | | | | 1 | | | | 5 | | |
| | ACA | TTG | ATG | TTC | TTA | TCA | AGC | TTT | TTC | ACC | AGC | CTT | GGG | TCC | TTC | ATT | 222 |
| | Thr | Leu | Met | Phe | Leu | Ser | Ser | Phe | Phe | Thr | Ser | Leu | Gly | Ser | Phe | Ile | |
| 20 | | | • | 10 | | | | | 15 | | | | | 20 | | | |
| | GTA | ATT | TGC | TCT | ATT | CTT | GGG | ACA | CAA | GCA | TGG | ATC | ACC | AGT | ACA | ATT | 270 |
| | Val | Ile | Cys | Ser | Ile | Leu | Gly | Thr | Gln | Ala | Trp | Ile | Thr | Ser | Thr | Ile | |
| | | | 25 | | | | | 30 | | | | | 35 | | | | |
| | | | | GAC | | | | | | | | | | | | | 318 |
| 25 | Ala | | Arg | Asp | Ser | Ala | Ser | Asn | Gly | Ser | Ile | Phe | Ile | Thr | Tyr | Gly | |
| | | 40 | | | | | 45 | | | | | 50 | | | | | |
| | | | | GGG | | | | | | | | | | | | | 366 |
| | | Phe | Arg | Gly | Glu | | Ser | Glu | Glu | Leu | | His | Gly | Leu | Ala | | |
| 20 | 55 | | | | | 60 | | | | | 65 | | | | | 70 | |
| 30 | | | | AAG | | | | | | | | | | | | | 414 |
| | PIG | гàг | ràs | Lys | | AIA | vaı | Leu | GIU | | Leu | Asn | Asn | Ser | | GIn | |
| | A A A | A (2) M | CEC | CAM | 75 mag | C TI C | 1 C M | A M.O. | 0.00 | 80 | 0.00 | 0.00 | 0.00 | 4.C.M | 85 | 4.50 | |
| | | | | CAT | | | | | | | | | | | | | 462 |
| 35 | Lys | 1111 | Leu | His 90 | ser | Val | 1111 | 116 | | Pne | Leu | VAI | Leu | | Leu | ite | |
| 33 | ACG | ፐርር | CTG | CTG | AGC. | ጥ ር ጥ | CCC | ጥጥጥ | 95 | ጥምር | ጥሉር | A A C | ۸۵۵ | 100 | ACC | A A C | 510 |
| | | | | Leu | | | | | | | | | | | | | 510 |
| | | JUL | 105 | acu. | Der | DEL | GIY | 110 | 1111 | FIIC | TAT | Vell | 115 | 116 | SET | usii | • |

| | | | | | | | • | | , (| 151 | | | | | | | |
|----|------|-------|-------|-------|-------|------|------|-------|-----|------|-----|------|------|------|------|-------|------|
| | CCT | TAC | CAG | ACA | TTC | CTG | GGG | CCG | ACG | GGG | GTG | TAC | ACC | TGG | AAC | GGG | 558 |
| | Pro | Tyr | Gln | Thr | Phe | Leu | Gly | Pro | Thr | Gly | Val | Tyr | Thr | Trp | Asn | Gly | |
| | | 120 | | | | | 125 | | | | | 130 | | | | | |
| | CTC | GGT | GCA | TCC | TTC | GTT | TTT | GTG | ACC | ATG | ATA | CTG | TTT | GTG | GCG | AAC | 606 |
| 5 | Leu | Gly | Ala | Ser | Phe | Val | Phe | Val | Thr | Met | Ile | Leu | Phe | Val | Ala | Asn | |
| | 135 | | | | | 140 | | | | | 145 | | | | | 150 | |
| | ACG | CAG | TCC | AAC | CAA | CTC | TCC | GAA | GAG | TTG | TTC | CAA | ATG | CTT | TAC | CCG | 654 |
| | Thr | Gln | Ser | Asn | Gln | Leu | Ser | Glu | Glu | Leu | Phe | Gln | Met | Leu | Tyr | Pro | |
| | | | | | 155 | | | | | 160 | | | | | 165 | | |
| 10 | GCA | ACC | ACC | AGT | AAA | GGA | ACG | ACC | CAC | AGT | TAC | GGA | TAC | TCG | TTC | TGG | 702 |
| | Ala | Thr | Thr | Ser | Lys | Gly | Thr | Thr | His | Ser | Tyr | Gly | Tyr | Ser | Phe | Trp | |
| • | | | | 170 | | | | | 175 | | | | | 180 | | | |
| | CTC | ATA | CTG | CTC | GTC | ATT | CTT | CTA | AAT | ATA | GTC | ACT | GTA | ACC | ATC | ATC | 750 |
| | Leu | Ile | Leu | Leu | Val | Ile | Leu | Leu | Asn | Ile | Val | Thr | Val | Thr | Ile | Ile | |
| 15 | | | 185 | | | | | 190 | | | | | 195 | | | | |
| | ATT | TTC | TAC | CAG | AAG | GCC | AGA | TAC | CAG | CGG | AAG | CAG | GAG | CAG | AGA | AAG | 798 |
| | Ile | Phe | Tyr | Gln | Lys | Ala | Arg | Tyr | Gln | Arg | Lys | Gln | Glu | Gln | Arg | Lys | |
| | | 200 | | | | | 205 | | | | | 210 | | | | | |
| | CCA | ATG | GAA | TAT | GCT | CCA | AGG | GAC | GGA | TTA | TTA | TTC | TGAA | TTCI | CT I | TCATC | 850 |
| 20 | Pro | Met | Glu | Tyr | Ala | Pro | Arg | Asp | Gly | Ile | Leu | Phe | | | | | |
| | 215 | | | | | 220 | | | | | 225 | | | | | | |
| | TCAT | PTTTG | GC G | TTG | CATC | IT A | GTAC | CATCA | GCC | CTGA | GTA | GTAA | CTGG | TT A | GCTI | CTCTG | 910 |
| | GACA | ATTC | CAG C | ATG | CAAT | G TG | ACTG | TCAT | CTG | TGAC | AGC | ATTI | GTGT | TT C | ATGA | CACTG | 970 |
| | TGT | CTTC | TAC | GAT | CTG7 | A CI | CCTG | AAAA | TTT | TTCC | CAC | AAGG | TTGG | GG A | AATG | AATGG | 1030 |
| 25 | GAAA | ATGTO | GC 1 | :GG | | | | | | | | | | | | | 1043 |
| | | | | | | | | • | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | (2) | INFO | RMAT | NOI | FOR | SEQ | ID N | 10: 5 | 2: | | | | | | | | |
| | | / 2 | \ CE | CITTO | 10E C | | | ** | | | | | | | | | |

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 972

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

35

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Liver

152

(D) CLONE NAME: HP10432

| (ix) | SEC | UENCE | CHARACTERISTICS | 3 : |
|------|-----|-------|-----------------|-----|
|------|-----|-------|-----------------|-----|

5

- (A) CHARACTERIZATION CODE: CDS
- (B) EXISTENCE POSITION: 29.. 418
 - (C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

| 10 | AGA | CAGC | GGC (| GGGC | GCAG | GA C | GTGC | | | | | | | | CGC Arg | | 52 |
|----|------|------------|-------|------|------|------|-----------|------|-------|--------------|------|----------------|------|------|------------|-------|------|
| | | | | | | | | | 1 | ***** | B | O ₁ | 5 | Dou | | •••• | |
| | TTG | CTG | CGG | CTC | CTC | GTG | CTG | GGG | СТС | TGG | CTG | GCG | TTG | СТС | CGC | TCC | 100 |
| | Leu | Leu | Arg | Leu | Leu | Val | Leu | Gly | Leu | Trp | Leu | Ala | Let | Lev | Arg | , Ser | |
| 15 | | 10 | | | | | 15 | | | | | 20 |) | | | | |
| | GTG | GCC | GGG | GAG | CAA | GCG | CCA | GGC | ACC | GCC | CCC | TGC | TCC | CGC | GGC | AGC | 148 |
| | Val | Ala | Gly | Glu | Gln | Ala | Pro | Gly | Thr | Ala | Pro | Cys | Ser | Arg | Gly | Ser | |
| | 25 | | | | | 30 | | | | | 35 | | | | | 40 | |
| | TCC | TGG | AGC | GCG | GAC | CTG | GAC | AAG | TGC | ATG | GAC | TGC | GCG | TCT | TGC | AGG | 196 |
| 20 | Ser | Trp | Ser | Ala | Asp | Leu | Asp | Lys | Cys | Met | Asp | Cys | Ala | Ser | Cys | Arg | |
| | | | | | 45 | | | | | 50 | | | | | 55 | i | |
| | | • | | | | | | | | | | | | | | CCT | 244 |
| • | Ala | Arg | Pro | | Ser | Asp | Phe | Cys | | Gly | Cys | Ala | Ala | | | Pro | |
| | | | | 60 | | | | | 65 | | | | | 70 | | | |
| 25 | _ | | | | | | | | | | | | | | | CTG | 292 |
| | Ala | Pro | | Arg | Leu | Leu | Trp | | Ile | Leu | Gly | Gly | | | Ser | Leu | |
| | | | 75 | | | | | 80 | | | | | 85 | | | | |
| | | | | | | | | | | | | | | | | TGC | 340 |
| 30 | Thr | | VAI | Leu | GTÄ | Leu | Leu | Ser | GIŻ | Phe | Leu | | _ | Arg | Arg | Cys | |
| ,, | cec | ,90 AGG | ACA | CAC | 440 | ጥጥር | 95 ACC | 400 | ccc | ለ ጥ ለ | CAC | 100 | | ccc | CCA | CAC | 388 |
| | | | | | | • | | | | | | | | | | Glu | 300 |
| | 105 | | nr g | GIU | Буз | 110 | 1111 | 1111 | FIO | 116 | 115 | GIU | 1111 | GIY | GLY | 120 | |
| | | | CCA | GCT | GTG | | СТС | ATC | CAG | тса | | ኮር ሞ (| GCCC | ርርፕር | CC A | CCGG | 440 |
| 35 | | | | | | | Leu | | | 1011 | J | .01 | 0000 | •••• | | | ,,,, |
| | , | -,- | | | 125 | | 200 | | 02 | | | | | | | | |
| | GGCI | CGCC | CA C | TCAT | | C AT | TCAT | CCA! | r TC: | raga(| GCCA | GTC | TCTG | CCT | CCCA | GACGC | 500 |
| | | | | | | | | | | | | | | | | TGAGG | |

153

620

680

CTGGGCCCAG GGTTCAGGGG AACCTTCCAA GGTGTCTGGT TGCCCTGCCT CTGGCTCCAG

AACAGAAAGG GAGCCTCACG CTGGCTCACA CAAAACAGCT GACACTGACT AAGGAACTGC

| | AGCATTTGCA CAGGGGAGGG GGGTGCCCTC CTTCCTAGAG GCCCTGGGGG CCAGGCTGAC | 740 |
|----|---|-----|
| | TTGGGGGGCA GACTTGACAC TAGGCCCCAC TCACTCAGAT GTCCTGAAAT TCCACCACGG | 800 |
| 5 | GGGTCACCCT GGGGGGTTAG GGACCTATTT TTAACACTAG GGGGCTGGCC CACTAGGAGG | 860 |
| | GCTGGCCCTA AGATACAGAC CCCCCAACT CCCCAAAGCG GGGAGGAGAT ATTTATTTTG | 920 |
| | GGGAGAGTTT GGAGGGGAGG GAGAATTTAT TAATAAAAGA ATCTTTAACT TT | 972 |
| | | |
| 10 | (2) INFORMATION FOR SEQ ID NO: 53: | |
| | (i) SEQUENCE CHARACTERISTICS: | |
| | (A) LENGTH: 695 | |
| | (B) TYPE: Nucleic acid | |
| | (C) STRANDEDNESS: Double | |
| 15 | (D) TOPOLOGY: Linear | |
| | (ii) SEQUENCE KIND: cDNA to mRNA | |
| | (vi) ORIGINAL SOURCE: | |
| | (A) ORGANISM: Homo sapiens | |
| 20 | (B) CELL KIND: Liver | |
| | (C) CELL LINE: | |
| | (D) CLONE NAME: HP10433 | |
| | (ix) SEQUENCE CHARACTERISTICS: | |
| 25 | (A) CHARACTERIZATION CODE: CDS | |
| | (B) EXISTENCE POSITION: 73 564 | |
| | (C) CHARACTERIZATION METHOD: E | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53: | |
| 30 | | |
| | AAGATTTCAG CTGCGGGACG GTCAGGGGAG ACCTCCAGGC GCAGGGAAGG ACGGCCAGGG | 60 |
| | TGACACGGAA GC ATG CGA CGG CTG CTG ATC CCT CTG GCC CTG TGG CTG GGC | 111 |
| | Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly | |
| | 1 5 10 | |
| 35 | GCG GTG GGC GTC GCC GAG CTC ACG GAA GCC CAG CGC CGG GGC | 159 |
| | Ala Val Gly Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Arg Gly | |
| | 15 20 25 | |
| | CTG CAG GTG GCC CTG GAG GAA TTT CAC AAG CAC CCG CCC GTG CAG TGG | 207 |

154

| | Leu | Gln | Val | Ala | Leu | Glu | Glu | Phe | His | Lys | His | Pro | Pro | Val | Gln | Trp . | |
|------|------|-------|---------|-------|-----|--------------|------|--------|------|------|------|------|------|-------|------|-------|-----|
| | 30 | | | | | 35 | | | | | 40 | | | • | | 45 | |
| | GCC | TTC | CAG | GAG | ACC | AGT | GTG | GAG | AGC | GCC | GTG | GAC | ACG | CCC | TTC | CCA | 255 |
| | Ala | Phe | Gln | Glu | Thr | Ser | Val | Glu | Ser | Ala | Val | Asp | Thr | Pro | Phe | Pro | |
| 5 | | | | | 50 | | | | | 55 | | | | | 60 | | |
| | GCT | GGA | ATA | TTT | GTG | AGG | CTG | GAA | TTT | AAG | CTG | CAG | CAG | ACA | AGC | TGC | 303 |
| | Ala | Gly | Ile | Phe | Val | Arg | Leu | Glu | Phe | Lys | Leu | Gln | Gln | Thr | Ser | Cys | |
| | | | | 65 | | | | | 70 | | | | | 75 | | | |
| | CGG | AAG | AGG | GAC | TGG | AAG | AAA | CCC | GAG | TGC | AAA | GTC | AGG | CCC | AAT | GGG | 351 |
| 10 . | Arg | Lys | Arg | Asp | Trp | Lys | Lys | Pro | G1u | Cys | Lys | Val | Arg | Pro | Asn | Gly | |
| | | | 80 | | | | | 85 | | | | | 90 | | | | |
| | AGG | AAA | CGG | AAA | TGC | CTG | GCC | TGC | ATC | AAA | CTG | GGC | TCT | GAG | GAC | AAA | 399 |
| | Arg | Lys | Arg | Lys | Cys | Leu | Ala | Cys | Ile | Lys | Leu | G1y | Ser | Glu | Asp | Lys | |
| | | 95 | | | | | 100 | | | | | 105 | | | | | |
| 15 | | | | | | GTC | | | | | | | | | | | 447 |
| | | Leu | Gly | Arg | Leu | Val | His | Cys | Pro | Ile | Glu | Thr | Gln | Val | Leu | Arg | |
| | 110 | | | | | 115 | | | | | 120 | | | | | 125 | |
| | | | | | | CAG | | | | | | | | | | | 495 |
| | Glu | Ala | Glu | Glu | His | Gln | Glu | Thr | Gln | Cys | Leu | Arg | Val | Gln | _ | Ala | |
| 20 | | | | | 130 | | | | | 135 | | | | | 140 | | |
| | | | | | | AGC | | | | | | | | | | | 543 |
| | Gly | Glu | Asp | | His | Ser | Phe | Tyr | | Pro | Gly | Gln | Phe | | Phe | Ser | |
| | | | | 145 | | | | | 150 | | | | | 155 | | | |
| | | | | | | AGC | TAAG | CCAG | CA C | TGAG | CTGC | G TG | GTGC | CTC | | | 590 |
| 25 | Lys | Ala | Leu | Pro | Arg | Ser | | | | | | | | | | | |
| | 0.00 | | 160 | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | AGA G | GACC | CCGTT | 650 |
| | CTA | rcccc | JAG (| CATO | ATA | AT AA | AGUI | GCTC | TCC | CAGC | TGC | CTCT | .C | | | | 695 |
| 30 | | | | | | | | | | | | | | | | | |
| 30 | (2) | TNE | NDM A T | rr or | FOR | CEO | TD N | 10 · E | ٠, . | | | | | | | | |
| | (2) | | | | | SEQ CHARA | | | | | | | | | | | |
| | | (- | וט ני | • | | TH: | | | .00; | | | | | | | | |
| | | | | | | e: Nu | | | -18 | | | | | | | | |
| 35 | | | | | | NDEI | | | | | | | | | | | |
| | | | | | | LOGY | | | | • | | | | | | | |
| | | | | (2) | | . 2001 | | a L | | | | | | | | | |

(ii) SEQUENCE KIND: cDNA to mRNA

| | | 7) | /i) (| ORIG | INAL | SOUI | RCE: | | | | | | | | | | • |
|----|-------------------------------|-----------|-------|------|---------|-------------|-----------|-------|-------|-------|-------|-------|-------|-------|-----|--------|-----|
| | | | | (A) | ORGA | MIS | 1: H | ото | sapi | ens | | | | | | | |
| | (B) CELL KIND: Stomach cancer | | | | | | | | | | | | | | | | |
| | | | | (D) | CLO | VE NA | AME: | HP1 | 0480 | | | | | | | | |
| 5 | | | | | | | | | | | | | | | | | |
| | | (: | ix) S | EQUI | ENCE | CHAI | RACTI | ERIS' | TICS | : | | | | | | | |
| | | | | (A) | CHAI | RACTI | ERIZA | ATIO | N COI | DE: (| CDS | | | | | | |
| | | | | (B) | EXIS | STEN | CE PO | OSIT: | ION: | 80. | . 663 | l | | | | | |
| | | | | (C) | CHAI | RACTI | ER I Z | ATIO | N ME | THOD | : E | | | | | • | |
| 10 | | | | | | | | | • | | | | | | | • | |
| | | () | ci) S | EQUI | ENCE | DESC | CRIP | rion | : SEC | Q ID | NO: | 54: | | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | GCTCGG | 60 |
| | CCC | CGCGC | CCG (| CCCG | CAAC | | | | | | | | | | | C TGC | 112 |
| 15 | • | | | | | Met | t Ile | e Ar | g Cys | s Gl | y Let | ı Ala | a Cy: | s Glu | | g Cys | |
| | | | | | | | L | | | | 5 | | | | 10 | | |
| | | | | | | | | | CTC | | | | | | | | 160 |
| | Arg | Trp | Ile | | Pro | Leu | Leu | Leu | Leu | Ser | Ala | Ile | Ala | | Asp | lle | |
| | | | | 15 | | | | | 20 | | | | | 25 | 200 | 0.10 | 000 |
| 20 | | | | | | | | | TTG | | | | | | | | 208 |
| | Ile | Ala | | Ala | Gly | Arg | Gly | | Leu | GIn | Ser | Ser | | HIS | GIÀ | GIN | |
| | | | 30 | 0.00 | | ma a | | 35 | maa | | 0.40 | 000 | 40 | ccc | ۸۵۵ | ccc | 256 |
| | | | | | | | | | TCC | | | | | | | | 230 |
| 25 | Tnr | | ser | Leu | Trp | Trp | Lys 50 | Cys | Ser | GIN | GIU | 55 | Gly | Gly | 261 | Gly | |
| 25 | TCC | 45 TAC | CAC | GAG | ccc | TOT | | AGC. | CTC | ልጥር | GAG | | GCG | тсс | GGT | AGA | 304 |
| | | | | | | | | | Leu | | | | | | | | |
| | 60 | -,- | o.u | 014 | - | 65 | | 001 | 204 | | 70 | | | | • | 75 | |
| | | GCG | GCT | GCC | | | | TGT | GGC | TTC | ATC | ATC | CTG | GTG | ATC | TGT | 352 |
| 30 | | | | | | | | | Gly | | | | | | | | |
| | | | | | 80 | | | • | | 85 | | | | | 90 | | |
| | TTC | ATC | CTC | TCC | TTC | TTC | GCC | CTC | TGT | GGA | ccc | CAG | ATG | CTT | GŤC | TTC | 400 |
| | | | | | | | | | Cys | | | | | | | | |
| | | | | 95 | | | | | 100 | | | | | 105 | | | |
| 35 | CTG | AGA | GTG | ATT | GGA | GGT | CTC | CTT | GCC | TTG | GCT | GCT | GTG | TTC | CAG | ATC | 448 |
| | Leu | Arg | Val | Ile | Gly | Gly | Leu | Leu | Ala | Leu | Ala | Ala | Val | Phe | Gln | Ile | |
| | | | 110 | | | | | 115 | | | | | 120 | | | | |
| | ATC | TCC | CTG | GTA | ATT | TAC | ccc | GTG | AAG | TAC | ACC | CAG | ACC | TTC | ACC | CTT | 496 |

| | Ile Ser Leu Val Ile Tyr Pro Val Lys Tyr Thr Gln Thr Phe Thr Leu | |
|----|---|------|
| | 125 130 135 | |
| | CAT GCC AAC CGT GCT GTC ACT TAC ATC TAT AAC TGG GCC TAC GGC TTT | 544 |
| | His Ala Asn Arg Ala Val Thr Tyr Ile Tyr Asn Trp Ala Tyr Gly Phe | |
| 5 | 140 145 150 155 | |
| | GGG TGG GCA GCC ACG ATT ATC CTG ATC GGC TGT GCC TTC TTC TGC | 592 |
| | Gly Trp Ala Ala Thr Ile Ile Leu Ile Gly Cys Ala Phe Phe Cys | |
| | 160 165 170 | |
| | TGC CTC CCC AAC TAC GAA GAT GAC CTT CTG GGC AAT GCC AAG CCC AGG | 640 |
| 10 | Cys Leu Pro Asn Tyr Glu Asp Asp Leu Leu Gly Asn Ala Lys Pro Arg | |
| | 175 180 185 | |
| | TAC TTC TAC ACA TCT GCC TA ACTTGGG AATGAATGTG GGAGAAAATC GCT | 690 |
| | Tyr Phe Tyr Thr Ser Ala | |
| | 190 | |
| 15 | GCTGCTGAGA TGGACTCCAG AAGAAGAAAC TGTTTCTCCA GGCGACTTTG AACCCATTTT | 750 |
| | TTGGCAGTGT TCATATTATT AAACTAGTCA AAAATGCTAA AATAATTTGG GAGAAAATAT | 810 |
| | TTTTTAAGTA GTGTTATAGT TTCATGTTTA TCTTTTATTA TGTTTTGTGA AGTTGTGTCT | 870 |
| | TTTCACTAAT TACCTATACT ATGCCAATAT TTCCTTATAT CTATCCATAA CATTTATACT | 930 |
| | ACATTTGTAA GAGAATATGC ACGTGAAACT TAACACTTTA TAAGGTAAAA ATGAGGTTTC | 990 |
| 20 | CAAGATTTAA TAATCTGATC AAGTTCTTGT TATTTCCAAA TAGAATGGAC TTGGTCTGTT | 1050 |
| | AAGGGCTAAG GAGAAGAGGA AGATAAGGTT AAAAGTTGTT AATGACCAAA CATTCTAAAA | 1110 |
| | GAAATGCAAA AAAAAAGTTT ATTTTCAAGC CTTCGAACTA TTTAAGGAAA GCAAAATCAT | 1170 |
| | TTCCTAAATG CATATCATTT GTGAGAATTT CTCATTAATA TCCTGAATCA TTCATTTCAG | 1230 |
| | CTAAGGCTTC ATGTTGACTC GATATGTCAT CTAGGAAAGT ACTATTTCAT GGTCCAAACC | 1290 |
| 25 | TGTTGCCATA GTTGGTAAGG CTTTCCTTTA AGTGTGAAAT ATTTAGATGA AATTTTCTCT | 1350 |
| | TTTAAAGTTC TTTATAGGGT TAGGGTGTGG GAAAATGCTA TATTAATAAA TCTGTAGTGT | 1410 |
| | TTTGTGTTTA TATGTTCAGA ACCAGAGTAG ACTGGATTGA AAGATGGACT GGGTCTAATT | 1470 |
| | TATCATGACT GATAGATCTG GTTAAGTTGT GTAGTAAAGC ATTAGGAGGG TCATTCTTGT | 1530 |
| | CACAAAAGTG CCACTAAAAC AGCCTCAGGA GAATAAATGA CTTGCTTTTC TAAATCTCAG | |
| 30 | GTTTATCTGG GCTCTATCAT ATAGACAGGC TTCTGATAGT TTGCAACTGT AAGCAGAAAC | |
| | CTACATATAG TTAAAATCCT GGTCTTTCTT GGTAAACAGA TTTTAAATGT CTGATATAAA | |
| | ACATGCCACA GGAGAATTCG GGGATTTGAG TTTCTCTGAA TAGCATATAT ATGATGCATC | |
| | GGATAGGTCA TTATGATTTT TTACCATTTC GACTTACATA ATGAAAACCA ATTCATTTTA | 1830 |
| | AATATCAGAT TATTATTTTG TAAGTTGTGG AAAAAGCTAA TTGTAGTTTT CATTATGAAG | 1890 |
| 35 | TTTTCCCAAT AAACCAGGTA TTCT | 1914 |

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CLAIMS

- A protein comprising an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ
 ID NOS: 1 to 18.
 - 2. A DNA encoding the protein according to claim 1.
- 3. A cDNA comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.
 - 4. A cDNA according to claim 3, which comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.
 - 5. An expression vector capable of in vitro translating the DNA according to any of claims 2 to 4 or expressing said DNA in an eukaryotic cell.

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6. A transformed eukaryotic cell capable of expressing the DNA according to any of claims 2 to 4 to produce the protein according to claim 1.

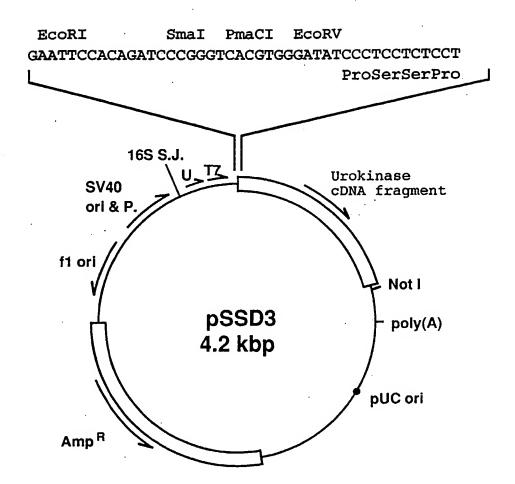
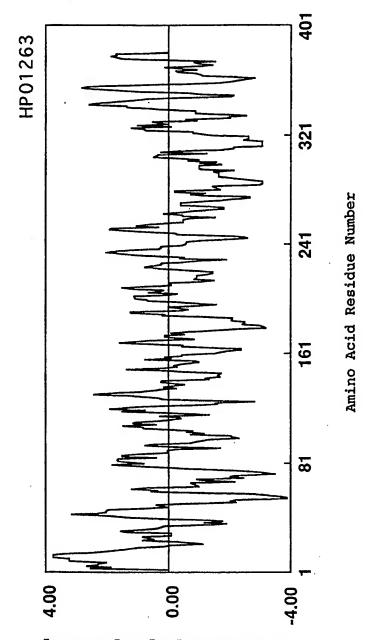


Fig.1



 ${\tt H} \lambda {\tt qxobyoptc} {\tt rf} \lambda \backslash {\tt H} \lambda {\tt qxobyr} {\tt ptc} {\tt rf} \lambda$

Fig.2

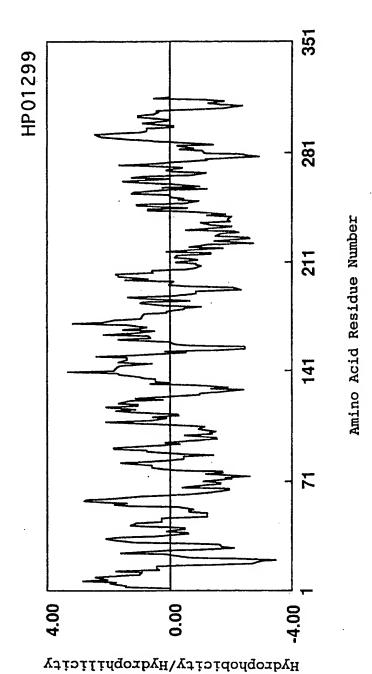


Fig.3

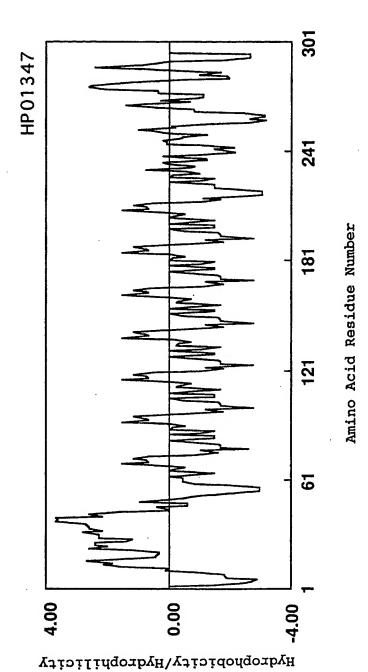


Fig.4

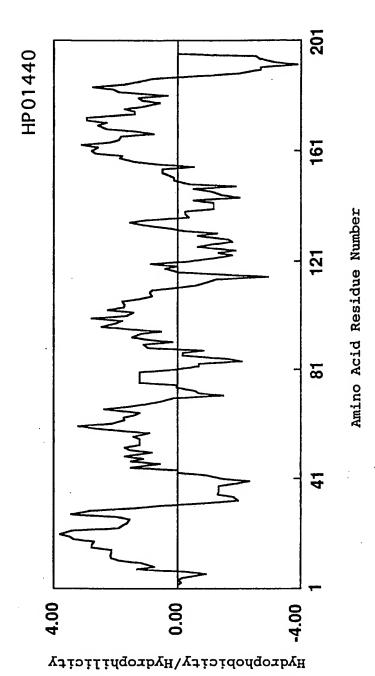
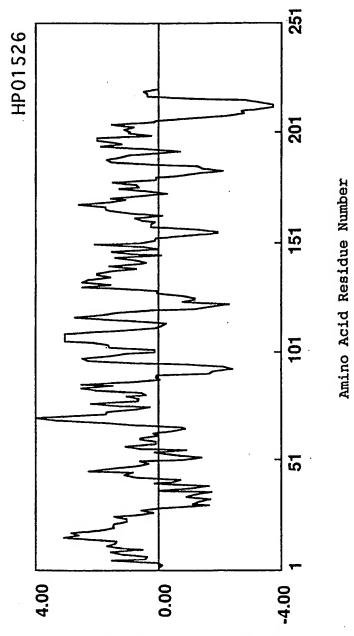


Fig.5



 ${\tt H} \lambda {\tt q} {\tt xobyoptc} {\tt rf} \lambda {\tt h} {\tt q} {\tt xoby} {\tt rf} {\tt rc} {\tt rf} \lambda$

Fig.6

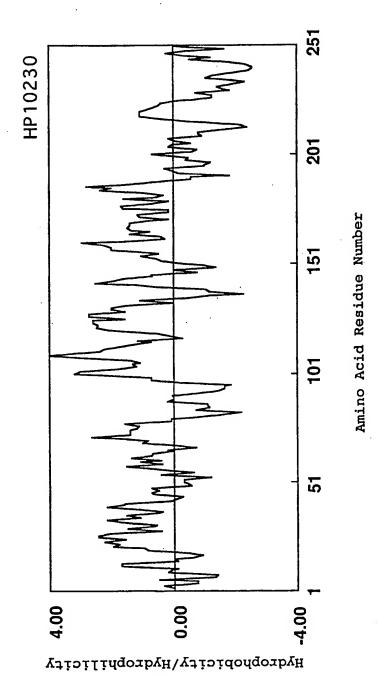


Fig.7

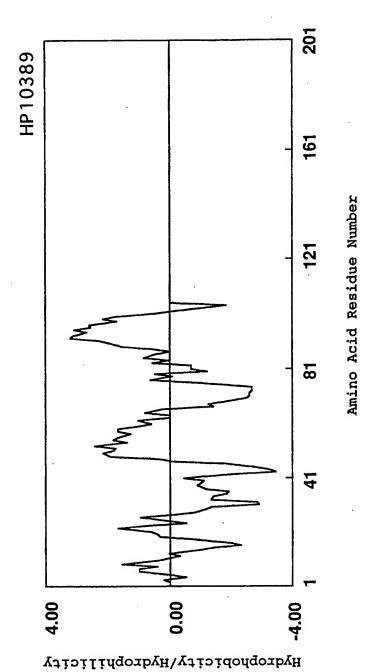


Fig.8

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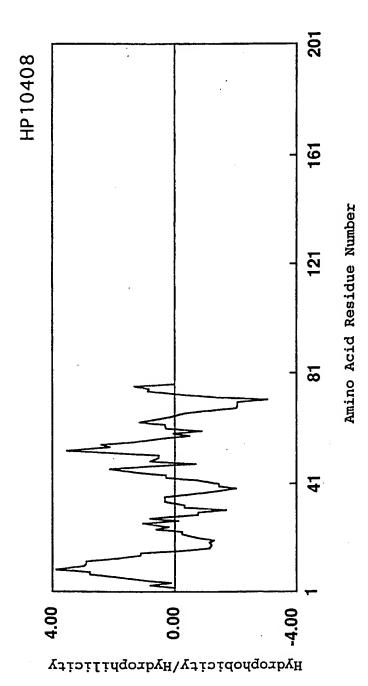


Fig.9

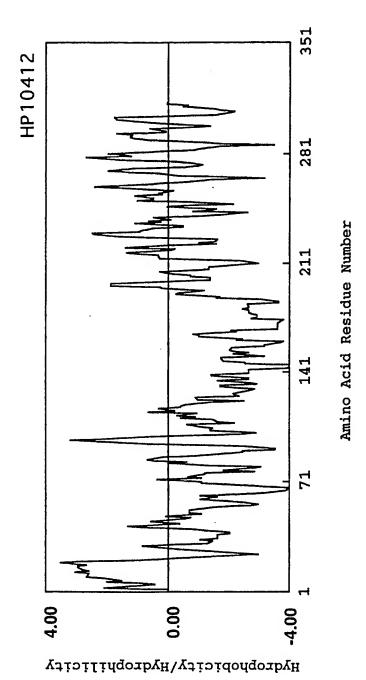


Fig.10

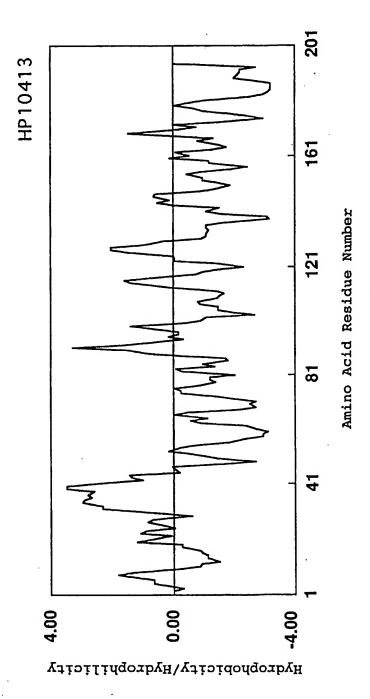


Fig.11

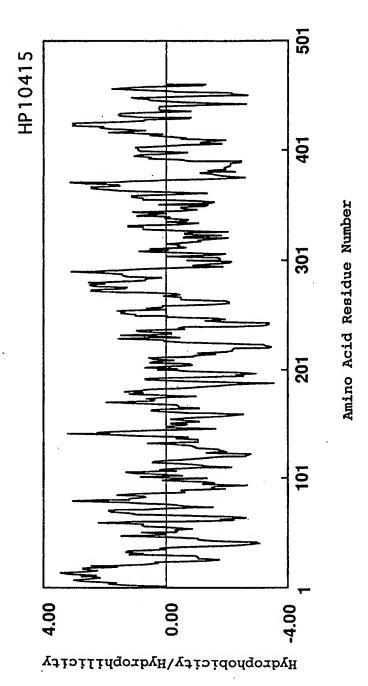


Fig.12

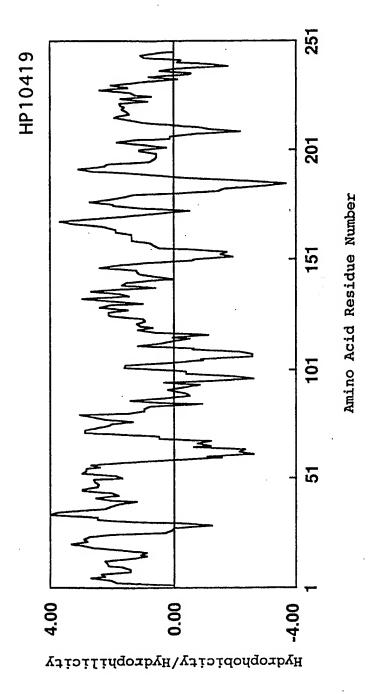


Fig.13

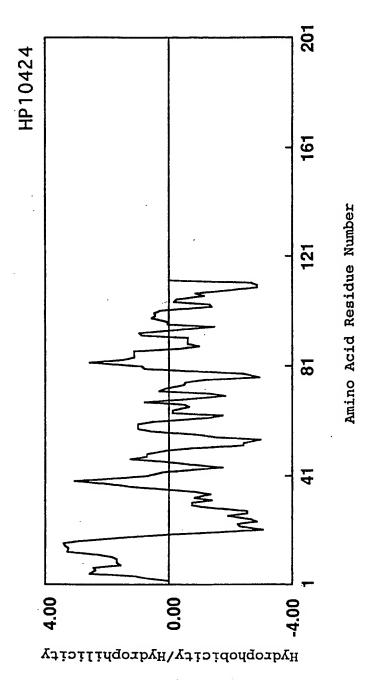


Fig.14

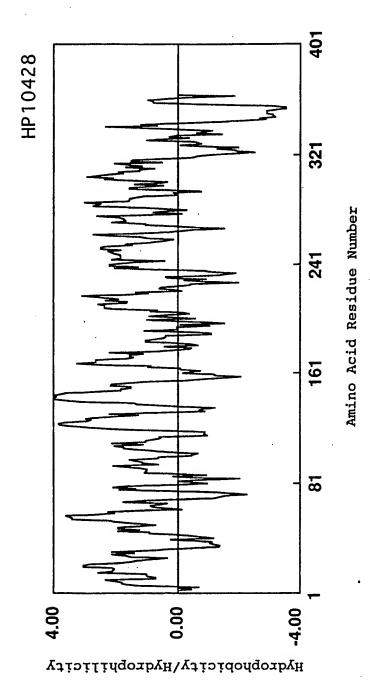


Fig.15

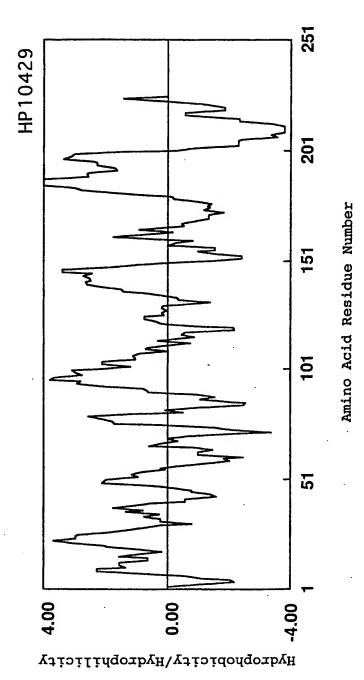


Fig.16

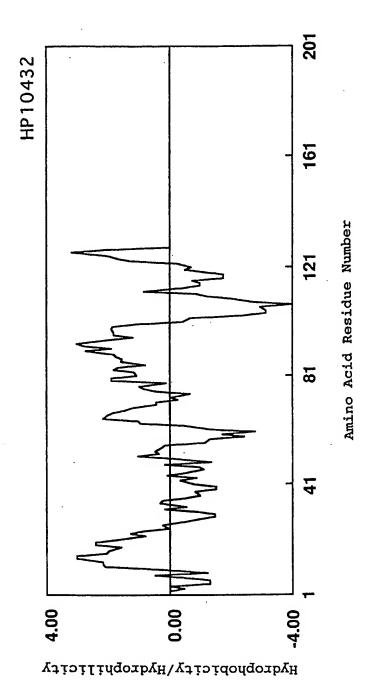
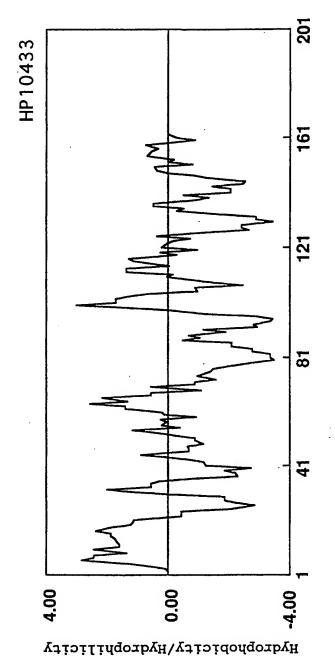


Fig.17



Amino Acid Residue Number

Fig.18

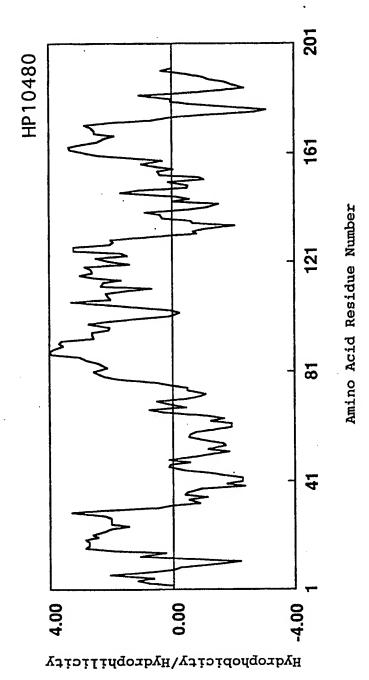


Fig.19